Book of Abstracts



JEEP2026

47th Conference on Phase Equilibria

Coimbra, 30 Sep - 2 Oct, 2026

JEEP2026

47th Conference on Phase Equilibria



30 September to 2 October 2026
Department of Chemistry
University of Coimbra
Portugal

Institutional Support

Departamento de Química
Universidade de Coimbra

Sociedade Portuguesa de Química

1 2 9 0
FACULDADE DE CIÊNCIAS E TECNOLOGIA
UNIVERSIDADE D COIMBRA

1 2 9 0
FACULDADE DE FARMÁCIA
UNIVERSIDADE D COIMBRA

Sponsors

fives
Fives ProSim

TECNIMEDE Group

specanalítica

setaram
KEP TECHNOLOGIES

Technobis

Grupo I.L.C.

Turismo Centro Portugal

CÂMARA MUNICIPAL DE COIMBRA

CONTENTS

Foreword	4
The long history of JEEP	5
JEEP2026 committees	6
Conference program	7
List of contributions	10
ABSTRACTS	19
Plenary lectures	20
Keynote lectures	25
Oral Communications	29
Poster Communications	53

FOREWORD

We are proud to welcome you to the 47th edition of JEEP – Congress on Phase Equilibria, hosted in the University of Coimbra, one of Europe's oldest universities. This Book of Abstracts is the scientific record of this conference, bringing together researchers and students devoted to the study of phase equilibria and their applications.

Over more than 40 years, JEEP has consolidated its importance to the dissemination of phase equilibrium research, bringing together disciplines as diverse as chemical engineering, materials science, thermodynamics, metallurgy, physical chemistry and computational modelling. The 2026 edition honors this tradition with worldwide contributions.

The University of Coimbra hosts a JEEP conference for the second time, after the success of the 41st edition in 2015.

This Book of Abstract compiles plenary and keynote lectures, oral communications and posters presented in the conference, covering a broad range of themes, from sustainable materials and processes to the optimization of chemical and industrial systems.

The Organizing Committee is indebted to all authors for the contributions submitted and the invited speakers for generously sharing their knowledge, and to the sponsors and partner institutions for their indispensable support in making this event possible.

We hope that this conference will also serve as an opportunity to strengthen collaborative networks and inspire new generations of researchers.

A warm welcome to everyone at JEEP2026 and to Coimbra.

Ermelinda Eusébio, João Canotilho, Mário Rosado

For the Organizing Committee of
JEEP2026 – 47th Congress on Phase Equilibria

THE LONG HISTORY OF JEEP

1st 1975 Marseille
2nd 1976 Lyon
3rd 1977 Montpellier
4th 1978 Grenoble
5th 1979 Chatenay-Malabry
6th 1980 Nancy
7th 1981 Genève
8th 1982 Orsay
9th 1983 Barcelona
10th 1984 Tours
11th 1985 Marseille
12th 1986 Bordeaux
13th 1987 Lyon
14th 1988 Montpellier
15th 1989 Grenoble
16th 1990 Marseille
17th 1991 Utrecht
18th 1992 Chatenay-Malabry
19th 1993 Barcelona
20th 1994 Bordeaux
21st 1995 Rouen
22nd 1996 Toulon
23rd 1997 Hammamet
24th 1998 Nancy
25th 1999 Annecy
26th 2000 Marseille
27th 2001 Montpellier
28th 2002 Agadir
29th 2003 Lyon
30th 2004 St Avold
31st 2005 Barcelona
32nd 2006 Rouen
33rd 2007 Villeurbanne
34th 2008 Marrakech
35th 2009 Annecy
36th 2010 Montpellier
37th 2011 St Avold
38th 2012 Rouen
39th 2013 Nancy
40th 2014 Lyon
41st 2015 Coimbra
42nd 2016 Paris
43rd 2017 Barcelona
44th 2019 Agadir
45th 2023 Rouen
46th 2025 Paris
47th 2026 Coimbra

JEEP2026 COMMITTEES

Scientific committee

Karine BALLERAT-BUSSEROLLES - Univ. Clermont-Auvergne, France
Marco CAMPESTRINI - Univ. PSL, France
João CANOTILHO - Univ. Coimbra, Portugal
Yohann CARTIGNY - Univ Rouen, France
Gérard COQUEREL - Univ. Rouen, France
João COUTINHO - Univ. Aveiro, Portugal
Ermelinda EUSÉBIO - Univ. Coimbra, Portugal
Christelle GOUTAUDIER – Univ. Lyon 1, France,
François GOUTENOIRE – Univ. Le Mans, France
Jean-Noël JAUBERT - ENSIC Nancy, France
Manuel MINAS da PIEDADE – Univ. Lisboa, Portugal
Ivo RIETVELD – Univ. Rouen, France
Mário ROSADO - Univ. Coimbra, Portugal

Organizing committee

Ermelinda EUSÉBIO
Mário ROSADO
João CANOTILHO
Mário CALVETE
Rui CARRILHO
Ricardo CASTRO
Carolina DOMINGOS
Teresa ROSEIRO
Mariette PEREIRA
João BAPTISTA
Rafael NEVES
Sara PINTO
João SANTOS
Nuno SANTOS



CONFERENCE PROGRAM

Day 1 · Wednesday 30 Sep

10:00 **Registration**

14:30 **Opening session**

M.E. Minas da Piedade

14:50 **PL1** Gérard Coquerel (U. Rouen)

Impact of symmetry and racemization on the shape of phase diagrams

15:40 **OC01** Agris Berzins (U. Latvia)

Steering polymorph selection with crystallization additives: lessons from solution and mechanochemical crystallization

16:00 **OC02** Cheng-long Stephan (U. Rouen)

Molecular-scale mechanism of γ-pyrazinamide stabilization by urea derivatives

16:20 **coffee break**

Y. Cartigny

16.50 **KL1** Christelle Goutaudier (Lyon 1 U.)

Phase diagrams: a powerfull tool for designing extraction strategies for high purity grade compounds

17:30 **OC03** Inês Vaz (U. Aveiro)

Unravelling the thermodynamics of lanthanide extraction using hydrophobic eutectic solvents

17:50 **OC04** Jorge Pereira (U. Coimbra)

From mixing to phase separation: hydrodynamic insights into cholinium chloride-based aqueous two-phase systems

18:10 **OC05** Gabriel Camilo (U. Aveiro)

Controlling phase equilibria and redox-species partitioning with NaSCN in ionic-liquid aqueous biphasic electrolytes

18:30 **OC06** Rúben Rocha (U. Coimbra)

Elesclomol-copper-loaded silk fibroin nanoparticles for glioblastoma therapy

18:50 **SUNSET BY THE MONDEGO**

Day 2 · Thursday 1 Oct

J. Coutinho

09.00 **PL2** Zhen Song (East China U.S.T.)

Machine learning-aided accurate prediction of pure-component and mixture properties

09:50 **OC07** Paulo Bonjour (Rio de Janeiro S.U.)

Hybrid molecular descriptor-based machine learning for PC-SAFT parameter

10:10 **OC08** Dinis Abranches (U. Aveiro)

AI-enabled discovery of deep eutectic solvents and their chemical space

10:30 **coffee break**

G. Coquerel

11:00 **KL2** Carlos Bernardes (U. Lisboa)

Energetics of crystalline organic materials: experimental and computational perspectives

11:40 **OC09** Gabin Gbabode (U. Rouen)

Structural investigation of the polymorphic transition of 1,3-dimethylurea

12:00 **OC10** Carlos Lima (U. Porto)

Thermodynamics of phase behavior and polymorphism in phenylacenes

12:20 **OC11** João Baptista (U. Coimbra)

Solid-state diversity in bisphenolic compounds: the roles of molecular flexibility and hydrogen bonding in polymorphism and solvation

12:40 **lunch**

M. Rosado

14:00 **PL3** Manuel Piñeiro (U. Vigo)

Molecular simulation of hydrates and hydroquinone organic clathrates

14:50 **OC12** Yohann Cartigny (U. Rouen)

Study of the solid-state landscape of the (an)hydrated forms of K7[SbW6O24], a new type of turn-off luminescence humidity sensors

15:10 **OC13** João Fabian (U. Aveiro)

Thermal and chemical stability of ionic liquids under high-temperature conditions

15:30 **SP** Specanalítica / Setaram

15:45 **Poster session | coffee-break**

G. Gbabode

16:40 **KL3** Eduardo Marques (U. Porto)

From phase equilibria to functional soft matter — towards responsive molecular delivery

17:20 **OC14** Maria João Moreno (U. Coimbra)

Molecular basis of trehalose-induced stabilization of phase coexistence in mixed phospholipid bilayers

17:40 **OC15** Margarida Pinhão (U. Aveiro)

Predicting partitioning of biomolecules in aqueous biphasic systems

18:00 **OC16** Alexandre Jorge (U. Coimbra)

Understanding the molecular interactions governing PEG/PPG aqueous two-phase system

19:30 **DINNER BY THE BOILERS**

Day 3 · Friday 2 Oct

C. Goutaudier

09.00 **PL4** João Coutinho (U. Aveiro)

The molecular mechanism of hydrotropic solvation: From Setschenow region to the formation of micelles

09:50 **OC17** Murilo Alcantara (U. Aveiro)

What's the best predictive model for ionic liquid screening? COSMO-SAC, COSMO-RS and GNN.

10:10 **OC18** Bruno Pinheiro (U. Porto)

From molecular structure to environmental mobility: predicting key properties of substituted benzenes

10:30 **coffee break**

C. Bernardes

11:00 **OC19** Elisa Collet (U. Rouen)

Crystal structure and behavior of the cocrystal salt (±)Ibuprofen2HK

11:20 **OC20** Kaoula Samadi (U. Burgos)

Effect of alkyl chain length on thermophysical properties of 2-ethoxyethanol + alcohol mixtures

11:40 **OC21** Aline Zambom (U. Aveiro)

Fractionation of winter savory essential oil model mixtures using imidazolium-based ionic liquids

12:00 **OC22** Mónia Martins (I.P. Bragança)

Solubility and solid-state behavior of metacetamol and paracetamol in pure and mixed solvents

12:20 **OC23** Bárbara Jesus (U. Lisboa)

Effect of water in the solubility of phenolics acids in diol-based eutectic solvents

12:50 **Awards & Closing**

13:00 **lunch bag**

LIST OF CONTRIBUTIONS

Plenary lectures

PL1 IMPACT OF SYMMETRY AND RACEMIZATION ON THE SHAPE OF PHASE DIAGRAMS
Gérard Coquerel
University of Rouen Normandy, France

PL2 MACHINE LEARNING-AIDED ACCURATE PREDICTION OF PURE-COMPONENT AND MIXTURE PROPERTIES
Zhen Song
East China University of Science and Technology, China

PL3 MOLECULAR SIMULATION OF HYDRATES AND HYDROQUINONE ORGANIC CLATHRATES
Manuel Piñeiro
University of Vigo, Spain

PL4 THE MOLECULAR MECHANISM OF HYDROTROPIC SOLVATION: FROM SETSCHENOW REGION TO THE FORMATION OF MICELLES
João Countinho
University of Aveiro, Portugal

Keynote lectures

KL1 PHASE DIAGRAMS: A POWERFULL TOOL FOR DESIGNING EXTRACTION STRATEGIES FOR HIGH PURITY GRADE COMPOUNDS
Christelle Goutaudier
Lyon I Claude Bernard University, France

KL2 ENERGETICS OF CRYSTALLINE ORGANIC MATERIALS: EXPERIMENTAL AND COMPUTATIONAL PERSPECTIVES
Carlos Bernardes
University of Lisbon, Portugal

KL3 FROM PHASE EQUILIBRIA TO FUNCTIONAL SOFT MATTER—TOWARDS RESPONSIVE MOLECULAR DELIVERY
Eduardo Marques
University of Porto, Portugal

Oral communications

OC01 STEERING POLYMORPH SELECTION WITH CRYSTALLIZATION ADDITIVES: LESSONS FROM SOLUTION AND MECHANOCHEMICAL CRYSTALLIZATION
A. Bērziņš, Z. Čerpakovska, A. Semjonova
University of Latvia, Latvia

OC02 MOLECULAR-SCALE MECHANISM OF γ-PYRAZINAMIDE STABILIZATION BY UREA DERIVATIVES
C. Stephan, G. Gbabode, I. B. Rietveld, A. Resta, A. Ø. Madsen
University of Roeun Normandy, France, Synchrotron SOLEIL, France and University of Copenhagen, Denmark

OC03 UNRAVELLING THE THERMODYNAMICS OF LANTHANIDE EXTRACTION USING HYDROPHOBIC EUTECTIC SOLVENTS
I. C. M. Vaz, M. Pinheiro, F. Olea, M. Bastos, L. M. N. B. F. Santos, J. A. P. Coutinho, N. Schaeffer
University of Aveiro, Portugal and University of Porto, Portugal

OC04 FROM MIXING TO PHASE SEPARATION: HYDRODYNAMIC INSIGHTS INTO CHOLINIUM CHLORIDE-BASED AQUEOUS TWO-PHASE SYSTEMS
A. M. S. Jorge, J. A. P. Coutinho, J. F. B. Pereira
University of Coimbra, Portugal and University of Aveiro, Portugal

OC05 CONTROLLING PHASE EQUILIBRIA AND REDOX-SPECIES PARTITIONING WITH NaSCN IN IONIC-LIQUID AQUEOUS BIPHASIC ELECTROLYTES
G. L. Camilo, M. L. Alcantara, A. M. Ferreira, J. A. P. Coutinho
University of Aveiro, Portugal

OC06 ELESCLOMOL-COPPER-LOADED SILK FIBROIN NANOPARTICLES FOR GLIOBLASTOMA THERAPY
R. Rocha, F. Branco, M. Mendes, A. Pais, C. Vitorino
University of Coimbra, Portugal

OC07 HYBRID MOLECULAR DESCRIPTOR-BASED MACHINE LEARNING FOR PC-SAFT PARAMETER
P. V. B. Bonjour, A. M. S. Jorge, J. F. B. Pereira
University of Coimbra, Portugal

OC08 AI-ENABLED DISCOVERY OF DEEP EUTECTIC SOLVENTS AND THEIR CHEMICAL SPACE
J. P. Santos, F. H. B. Sosa, D. O. Abranches, J. A. P. Coutinho
University of Aveiro, Portugal

OC09 STRUCTURAL INVESTIGATION OF THE POLYMORPHIC TRANSITION OF 1,3-DIMETHYLUREA
G. Gbabode, M. Sulli
University of Roeun Normandy, France and University of Florence, Italy

OC10 THERMODYNAMICS OF PHASE BEHAVIOR AND POLYMORPHISM IN PHENYLACENES
C. F. R. A. C. Lima, C. S. T. Pinto, F. V. Ribeiro, L. M. N. B. F. Santos,
J. C. S. Costa
University of Porto, Portugal

OC11 SOLID-STATE DIVERSITY IN BISPHENOLIC COMPOUNDS: THE ROLES OF MOLECULAR FLEXIBILITY AND HYDROGEN BONDING IN POLYMORPHISM AND SOLVATION
J. A. Baptista, R. A. E. Castro, E. Fantechi, L. Chelazzi, S. Ciattini,
M. T. S. Rosado, M. E. S. Eusébio
University of Coimbra, Portugal and University of Florence, Italy

OC12 STUDY OF THE SOLID-STATE LANDSCAPE OF THE (AN)HYDRATED FORMS OF $K_7[SbW_6O_{24}]$, A NEW TYPE OF TURN-OFF LUMINESCENCE HUMIDITY SENSORS.
S. Kissage-Silva, L. Papin, M. Sanselme, N. Couvrat,
R. Dessapt, Y. Cartigny
University of Roeun Normandy, France and Nantes University, France

OC13 THERMAL AND CHEMICAL STABILITY OF IONIC LIQUIDS UNDER HIGH-TEMPERATURE CONDITIONS
J. Fabian, M. L. Alcantara, C. F. H. B. Sosa, J. A.P. Coutinho
University of Aveiro, Portugal

OC14 MOLECULAR BASIS OF TREHALOSE-INDUCED STABILIZATION OF PHASE COEXISTENCE IN MIXED PHOSPHOLIPID BILAYERS
A. M. Alves, M. J. Moreno, L. M. S. Loura
University of Coimbra, Portugal

OC15 PREDICTING PARTITIONING OF BIOMOLECULES IN AQUEOUS BIPHASIC SYSTEMS
M. D. Pinhão, E. V. Capela, J. A. P. Coutinho, M. G. Freire, D. O. Abranches
University of Aveiro, Portugal

OC16 UNDERSTANDING THE MOLECULAR INTERACTIONS GOVERNING PEG/PPG AQUEOUS TWO-PHASE SYSTEM FORMATION
A. M. S. Jorge, G. M. C. Silva, J. A. P. Coutinho, J. F. B. Pereira
University of Coimbra, Portugal and University of Aveiro, Portugal

OC17 WHAT'S THE BEST PREDICTIVE MODEL FOR IONIC LIQUID SCREENING? COSMO-SAC, COSMO-RS AND GNN
M. L. Alcantara, E. T. Souza Jr., J. G. Rittig, R. de P. Soares, P. B. Staudt, P. Schwaller, J. A. P. Coutinho
University of Aveiro, Portugal, Federal University of Rio Grande do Sul, Brazil and EPFL, Switzerland

OC18 FROM MOLECULAR STRUCTURE TO ENVIRONMENTAL MOBILITY: PREDICTING KEY PROPERTIES OF SUBSTITUTED BENZENES
B. Pinheiro, A. Almeida, M. Monte
University of Porto, Portugal

OC19 CRYSTAL STRUCTURE AND BEHAVIOR OF THE COCRYSTAL SALT (±)IBUPROFEN$_2$HK
E. Collet Salvet, M. Sanselme, Y. Cartigny, R. Texeira, C. Rougeot, G. Coquerel
University of Roeun Normandy, France and Sanofi's Analytical Characterization Laboratories, France

OC20 EFFECT OF ALKYL CHAIN LENGTH ON THERMOPHYSICAL PROPERTIES OF 2-ETHOXYETHANOL + ALCOHOL MIXTURES
K. Samadi, M. Lifi, N. Muñoz Rujas, F. Aguilar, F. E. M'hamdi Alaoui
University of Abdelmalek Essaadi, Morocco and University of Burgos, Spain

OC21 FRACTIONATION OF WINTER SAVORY ESSENTIAL OIL MODEL MIXTURES USING IMIDAZOLIUM-BASED IONIC LIQUIDS
A. Zambom, O. Ferreira, J. A. P. Coutinho, S. P. Pinho, S. M. Vilas-Boas, H. Rodríguez
University of Santiago de Compostela, Spain, Polytechnic Institute of Bragança, Portugal and University of Aveiro, Portugal

OC22 SOLUBILITY AND SOLID-STATE BEHAVIOR OF METACETAMOL AND PARACETAMOL IN PURE AND MIXED SOLVENTS
M. A. R. Martins, A. Zambom, L. G. Arantes, P. Brandão, J. A. P. Coutinho, O. Ferreira, S. P. Pinho
Polytechnic Institute of Bragança, Portugal and University of Aveiro, Portugal

OC23 EFFECT OF WATER IN THE SOLUBILITY OF PHENOLICS ACIDS IN DIOL-BASED EUTECTIC SOLVENTS
B. C. Jesus, I. M. Marrucho, N. Galamba, M. Miquel-Gonzalez, C. A. Martins
University of Lisbon, Portugal, Polytechinic University of Madrid, Spain and Portugal and MARE-IPLeiria, Portugal

Poster communications

P01 EFFECT OF PHENYLATION ON THE PHASE BEHAVIOR OF PHENANTHRENE DERIVATIVES
C. S. T. Pinto, L. M. N. B. F. Santos, J. C. S. Costa, C. F. R. A. C. Lima

P02 FUNCTIONAL GROUP EFFECTS ON LEFLUNOMIDE COCRYSTAL FORMATION: AMIDE VERSUS CARBOXYLIC ACID COFORMERS
N. A. S. Santos, J. A. Baptista, J. Canotilho, M. E. S. Eusébio, R. A. E. Castro, T. M. R. Maria

P03 PHASE BEHAVIOR STUDY OF LARGE PHENYL ACENES: PHENYLCHRYSENE AND PHENYLTRIPHENYLENE
A. P. Ferreira, L. M. N. B. F. Santos, C. F. R. A. C. Lima

P04 EFFECT OF A DEEP EUTECTIC SOLVENT AND ITS CONSTITUENTS ON TETRAHYDROFURAN CLATHRATE HYDRATES NUCLEATION
A. P. Ferreira, C. E. S. Bernardes, R. G. Simões, M. Tariq

P05 INFLUENCE OF SOLVENT ON THE FORMATION OF DISTINCT MEFENAMIC ACID-L-ARGININE SOLID FORMS
J. G. Santos, R. A. E. Castro, F. J. Caires

P06 STRUCTURAL AND THERMAL CHARACTERIZATION OF PHARMACEUTICAL COCRYSTALS AND CO-AMORPHOUS SYSTEMS
S. P. Gonçalves, P. S. P. Silva, M. R. Silva, M. T. S. Rosado, T. M. R. Maria, M. E. S. Eusébio

P07 THEDES PHASE TRANSITION DYNAMICS FOR ENHANCED TUBERCULOSIS TREATMENT
T. Alves, D. Alves, A. Granja, M. Borges, C. Nunes, S. Reis, M. Sarraguça

P09 SOLID-STATE CHARACTERISATION OF AROMATIC AZIDES: FROM CRYOGENIC CRYSTALLISATION TO PERIODIC DFT MODELLING
R. R. Neves, J. A. Paixão, C. M. Nunes, M. T. S. Rosado

P10 EXPERIMENTAL AND NUMERICAL STUDY OF TERNARY SYSTEMS MSO_4-M'SO_4-H_2O (M, M' = Li_2, Ni, Co)
N. Patry, A. Lassin, L. Andre, Y. Cartigny, N. Couvrat

P11 STRUCTURE, STABILITY AND SOLUBILITY OF A NEW MONOMETHYL FUMARATE:NICOTINAMIDE BICOMPONENT CRYSTAL
M. F. M. Piedade, R. L. Mané, R. G. Simões, M. E. Minas da Piedade

P12 MONOETHYL FUMARATE IN WATER: FROM SOLUBILITY CURVE TO LIQUID-LIQUID PHASE SEPARATION
D. N. G. Palma, R. G. Simões, C. E. S. Bernardes, M. E. Minas da Piedade

P13 DEEP EUTECTIC SOLVENTS AS TUNABLE MEDIA FOR ENHANCING THE SOLUBILITY OF QUERCETIN
R. Costa, R. Maduro, S. Reis, M. Passos, M. Sarraguça

P14 MOLECULAR DYNAMICS OF CARBONIC ANHYDRASE II IN CHOLINE:UREA-BASED DEEP EUTECTIC SOLVENTS
D. J. M. Agostinho, M. M. Pereira, M. E. Ghica

P15 ACCELERATING OPENCOSMO-RS WITH GRAPH CONVOLUTIONAL NETWORKS
R A. F. Serrano, S. Müller, I. Smirnova, J. A. P. Coutinho, D. O. Abranches

P16 PHASE EQUILIBRIUM PROPERTIES OF BINARY SYSTEMS (FURFURAL + ALCOHOLS) AT SEVERAL TEMPERATURES
N. Chiali, A. Negadi, J. Jose, I. Mokbel, L. Negadi

P17 MODELING EXCESS MOLAR ENTHALPIES OF DIMETHYL CARBONATE WITH EIGHT HYDROCARBONS
N. Chiali, A. Negadi, J. Jose, L. Negadi

P18 THERMOPHYSICAL CHARACTERIZATION OF DMSO-BASED BINARY MIXTURES
F. Ouaar, N. Chiali, A. Negadi , L. Negadi

P19 EXPERIMENTAL EXCESS MOLAR ENTHALPIES AND THERMODYNAMIC ANALYSIS OF BINARY MIXTURES OF 1-BUTANOL WITH GLYCOL ETHERS
K. Samadi, M. Lifi, H. Lifi, F. Aguilar, F. E. M'hamdi Alaoui

P21 MEASUREMENTS AND MODELING OF THE PHYSICO-CHEMICAL PROPERTIES OF 1,2-DIMETHOXYETHANE AND ITS BINARY MIXTURES WITH VARIOUS ALCOHOLS
N. L. Benkalfat-Seladji, N. C. Baba-Ahmed, A. Belabbaci, A. Negadi, L. Negadi

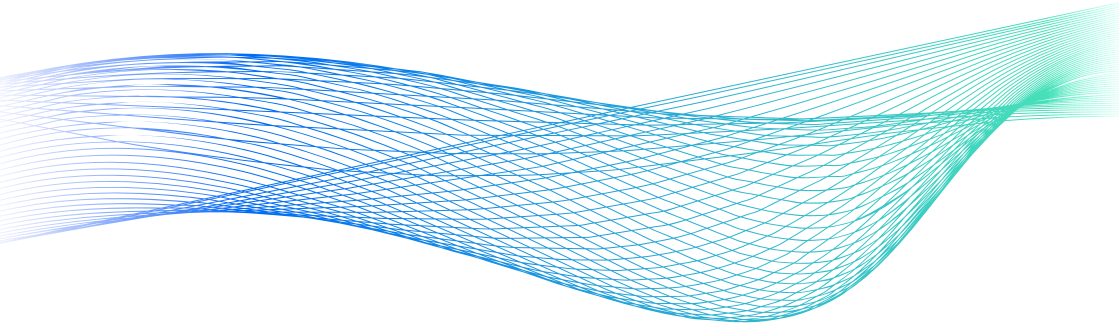
P22 THERMODYNAMIC, ULTRASONIC, AND TRANSPORT STUDY OF BINARY MIXTURES CONTAINING 1-HEXENE AND ALCOHOLS AT (293.15 - 303.15)K
A. Belabbaci, K. N. Abdellaoui, A. Ayad, A. Negadi, L. Negadi

P23 EXCESS THERMODYNAMIC AND TRANSPORT PROPERTIES OF BINARY MIXTURES OF FURFURAL OR FURFURYL ALCOHOL WITH 1 PROPANOL AND 2-PROPANOL
A. Ayad, Z. Boudellal, A. Belabbaci, A. Negadi, L. Negadi

P24 THERMOPHYSICAL PROPERTIES OF BINARY SYSTEMS CONTAINING 2-ETHOXYETHANOL AND ALCOHOLS
N. L. Benkelfat-Seladji, N. Chiali-BabaAhmed, A. Ayad, A. Negadi, L. Negadi

ABSTRACTS

PLENARY LECTURES



Impact of symmetry and racemization on the shape of phase diagrams

G. Coquerel
Univ Rouen Normandie, SMS, UR 3233, F-76000 Rouen, France
e-mail:gerard.coquerel@univ-rouen.frt

Starting from Gibbs phase rule, a perfect mirror symmetry between components will be introduced. The main consequence will be the modification of the phase rule (the so-called: Gibbs- Scott rule) and the apparition of a mirror symmetry in the phase diagrams. For instance, a binary system of pure enantiomers under constant pressure exhibits a mirror symmetry along the racemic composition – temperature axis. If the enantiomers have two enantiotropic forms and there is no stable racemic compound (i.e. the conglomerate is thermodynamically stable), it will result in a four-phase invariant.
When adding racemization in addition to the mirror symmetry between the components, the system has an 'odd' behavior. Indeed, numerous, experiments in inorganic chemistry as well as with organic components have shown that the system will undergo a spontaneous symmetry breaking. Counter intuitively with regard to entropy, sooner or later the system will be enriched in a single enantiomer most of the time at the end of the evolution, the solid phase exhibits 100% enantiomeric purity. The kinetics aspect of the enantio-enrichment depends upon process parameters. Indeed, when a suspension of enantiomers, crystallizing as a conglomerate with fast racemization in solution, is subjected to a flux of energy, the system spontaneously evolves towards homochirality. These fluxes of energy can be quite diverse: without being exhaustive on can cite: mechanical, thermal, pressure, ultra-sounds, light, microwaves, etc. can be used alone or in combination with beneficial agonist effects.
This spontaneous evolution leads to reconsider many phase diagrams with molecular chirality but also with supramolecular chirality.

References

(1) Viedma, C. *Phys. Rev. Lett.* 2005, **94**, 065504.
(2) Suwannasang, K.; Flood, A.; Rougeot, C.; Coquerel, G. *Cryst. Growth. Des*. 2013, **13**, 3498−3504.
(3) Cameli, F.; Xiouras, C.; Stefanidis, G.D. *Cryst. Eng. Comm.* 2018, **20**, 2897−2901.

Machine learning-aided accurate prediction of pure-component and mixture properties

Zhen Song[a,*]
[a] *East China University of Science and Technology, 130 Meilong Road, Shanghai, China*
[*] *e-mail: songz@ecust.edu.cn*

Accurate prediction of pure-component and mixture physicochemical properties is at the heart of chemical process simulation, and solvent screening. However, experimental datasets are usually sparse, making pure data-driven models prone to overfitting and poor generalization. This talk presents tailored machine learning (ML) strategies for accurate property prediction under limited-data conditions.

For pure-component properties, three approaches are developed. First, a dual-perspective ML framework combining regression and classification tasks is developed, enabling simultaneous use of quantitative measurements and qualitative property ranges.[1] Second, a transfer learning scheme from homologous dataset is proposed, where knowledge from data-abundant similar chemical systems could strengthen model's extrapolation performance.[2] Third, a universal pre-training and fine-tuning strategy learns general chemical representations from large-scale unlabeled molecular data and subsequently adapts them using small labeled datasets.[3] For mixture properties, where thermodynamic nonlinearity and data sparsity are more severe, two complementary strategies are proposed. A recommendation-system-inspired approach extracts latent correlations from sparse binary interaction matrices for mixture property prediction[4], while a physics-informed machine learning framework embeds thermodynamic constraints into data-driven models, reducing data dependence and enabling robust prediction of phase equilibria and solubility across broad operating ranges.[5] An open web platform named *ai4solvents*, is implemented, covering property prediction for molecular solvents, ionic liquids (ILs), deep eutectic solvents, and refrigerants.[6] Two representative application cases further verify the effectiveness of the proposed methods and platform, one is the screening of ILs to engineering interfacial polymerization for COF membrane synthesis,[7] and the other is screening effective $LiNO_3$ solvents toward dilute nitrate electrolytes for all-climate batteries.[5]

References

(1) Zhu, Q.; Qiu, Y.; Chen, G., et al. *Adv. Sci.* 2025, **12**, e11667.
(2) Qiu, Y.; Chen, J. ; Xie, K., et al. *Chem. Eng. Sci.* 2024, **300**, 120559.
(3) Qiu, Y.; Song, Z.; Chen, G., et al. *Digit. Discov.* 2025, **4** 1505–1517.
(4) Chen, G.; Song, Z.; Qi, Z., et al. *AIChE J.* 2025, **67**, e17171.
(5) You, H.; Chen, J.; Li, R., et al. *Joule* 2026, 102548.
(6) http://ai4solvents.com/
(7) Wang, K.; Cao, W.; Xie, K., et al. *AIChE J.* 2026, **72**, e70186.

Molecular simulation of hydrates and hydroquinone organic clathrates

M. M. Piñeiro[a,*]
[a] *Departamento de Física Aplicada, Universidade de Vigo,*
[*] *e-mail: mmpineiro@uvigo.es*

Organic clathrates are non-stoichiometric solid inclusion compounds where a crystalline network of host molecules can store small guest molecules in the cavities left inside its structure. If the host molecule is water, these compounds are simply termed as hydrates. Over the last decades, clathrates have become a subject of increasing research interest due to the number of applications where they are involved. The potential recuperation of the huge amounts of methane trapped in hydrate deposits in nature was one of the first motivations for these studies, but many other potential applications have been pointed out, as for instance preferential gas separation and adsorption, CO_2 sequestration, water desalination, H_2 storage, and a few others. The complex multiphasic nature of these systems poses a challenge for the theoretical description of their phase equilibria, thermophysical and transport properties, dynamics, and microscopic structure. Macroscopic thermodynamic approaches provide accurate estimations only for simple cases but fail to reproduce even qualitatively the behavior of more realistic samples. In this context, atomic scale approaches as *ab initio* calculations, or classical molecular simulations, provide a powerful framework to estimate structural and thermodynamic properties of these clathrates. In this presentation, a review of some of our research works in this field is presented, focusing in two particular case studies: the structure and phase equilibria of methane hydrates under oceanic conditions, and the potential use of hydroquinone clathrates as H_2 storage media.

The molecular mechanism of hydrotropic solvation: from Setschenow region to the formation of micelles

J. A. P. Coutinho[a,*], D. O. Abranches[a], S. P. Pinho[b], E. E. Fileti[c]
[a] *CICECO – Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810-193, Aveiro, Portugal*
[b] *CIMO, LA SusTEC, Instituto Politécnico de Bragança, 5300-253 Bragança, Portugal*
[c] *Instituto de Ciência e Tecnologia, Universidade Federal de São Paulo, 12247-014, São José dos Campos, SP, Brazil*
[*] *e-mail: jcoutinho@ua.pt*

Hydrotropes and surfactants are commonly employed to enhance the aqueous solubility of hydrophobic compounds, and they are traditionally regarded as distinct classes based on the assumption that surfactants solubilize via micelle formation whereas hydrotropes do not. In the first part of this communication, this distinction is critically examined by systematically investigating the solubilization of carbamazepine in aqueous solutions of two homologous families: sodium sulfates and sodium sulfonates, spanning species from inorganic salts to classical surfactants. Across these families, solubility enhancement increases monotonically with the apolar volume of the anion[1], with densely charged ions inducing salting-out and amphiphilic compounds promoting salting-in. Analysis of the dilute concentration regime using Setschenow constants reveals a continuous trend encompassing hydrotropes and surfactants, with no separation between them.

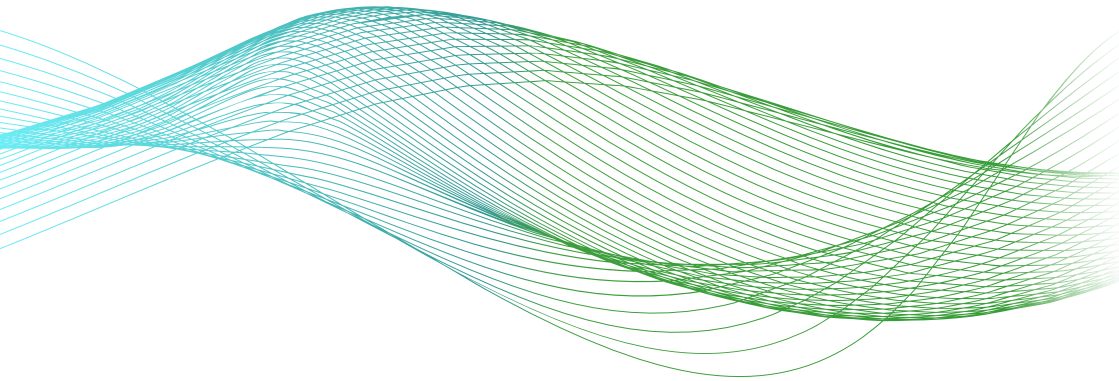
At higher amphiphile concentrations, deviations from linear behavior define critical aggregation concentrations that correlate systematically with anion apolarity among hydrotropes and surfactants, and align closely with reported critical micelle concentrations. These results establish a unified framework in which hydrotropes and surfactants follow the same structural and thermodynamic principles, supporting a continuum view of solubilizing agents.

The mechanisms of enhanced solubility on these systems are further highlighted by molecular dynamic simulations, and, in the final part of this communication, it will be shown how other phenomena, apparently unrelated, such as the impact of dissolved gases on the transport properties of electrolytes[2], or the solubility of gases in aqueous solutions of ionic liquids, can be understood under the light of the aggregation of amphiphiles in water around an apolar compound.

Acknowledgments
The authors are grateful to FCT, Portugal, for financial support through national funds FCT/MCTES (PIDDAC) to CICECO from projects UID/50011/2025 and LA/P/0006/2020, and CIMO UID/00690/2025 and SusTEC, LA/P/0007/2020.

References
(1) Soares, B.P., et al. *ACS Sustain. Chem. Eng.,* 2020, **8**, 5742.
(2) Fileti, E.E.; Abranches, D.O.; Coutinho, J.A.P. *J. Phys Chem B*, 2026, **130**, 5059.

KEYNOTE LECTURES



Phase diagrams: a powerfull tool for designing extraction strategies for high purity grade compounds

C. Goutaudier[a,*]

[a] *Lyon 1 Université, Laboratoire Multimatériaux et Interfaces, UMR CNRS 5615, Villeurbanne, France*

[*] *e-mail: christelle.goutaudier@univ-lyon1.fr*

The various stages of a chemical synthesis, as well as the occurrence of secondary reactions, can lead to complex mixtures in which the target compound may be present in very small amounts. Furthermore, it is rare for a specific extraction process to yield, in a single step, a pure product with the required qualities and the specified degree of purity for industrial applications. For high added value compounds, it is necessary to implement an appropriate extraction and purification strategy. The approach is exclusively based on knowledge and exploitation of phase diagrams, which form the basis for unit operations in phase separation. The key research tools deployed are, on one hand, experimental measurements and, on the other hand, modelling of the equilibria involved in order to determine the yield of each step of extraction. The relevance of this approach will be demonstrated through two examples that show concrete applications in the fields of space technology and electronics and that require high levels of purity.

Energetics of crystalline organic materials: experimental and computational perspectives

C. E. S. Bernardes*
Centro de Química Estrutural, Institute of Molecular Sciences, Faculdade de Ciências, Universidade de Lisboa, Campo Grande, 1749-016 Lisboa, Portugal
**e-mail: cebernardes@ciencias.ulisboa.pt*

The physical properties of organic substances, such as solubility and melting point, are intimately related to their molecular assembly in the solid state. Consequently, in recent decades, there has been significant interest in developing methodologies to modify the organization of molecules in crystals, either by altering their packing arrangement (a phenomenon known as polymorphism) or by incorporating other compatible molecules (forming multicomponent materials), to change and control the properties of substances. As a result, the investigation of structure-property relationships has become a significant topic of interest in many industries, particularly in the pharmaceutical sector.

Structure-property relationships are intrinsically related to our ability to control and rationalize the intermolecular forces present in crystalline structures. This can be achieved by employing both experimental and theoretical methods. Experimentally, it is possible, for example, to use calorimetric methods to measure the lattice enthalpy of a substance or evaluate lattice-energy differences between solid phases, providing a quantitative measure of the energetic contribution of intermolecular interactions. These results are also crucial for testing and validating theoretical methods and for assessing their ability to predict the properties of compounds.

In this communication, an overview of our recent research on the interplay between theoretical and experimental methods in the investigation of the properties of materials, particularly active pharmaceutical ingredients (APIs), will be presented.

Acknowledgments
This work was supported by Fundação para a Ciência e Tecnologia (FCT) through projects UID/00100/2025(https://doi.org/10.54499/UID/00100/2025),UID/PRR/00100/2025(https://doi.org/10.54499/UID/PRR/00100/2025),LA/P/0056/2020(https://doi.org/10.54499/LA/P/0056/2020), 2023.12474.PEX (https://doi.org/10.54499/2023.12474.PEX), and 2023.15441.TENURE.004/CP00003/CT00002.

From phase equilibria to functional soft matter—towards responsive molecular delivery

E. F. Marques
CIQUP-IMS, Faculty of Sciences, University of Porto, Porto, Portugal
*e-mail: efmarque@fc.up.pt

Amphiphilic molecules form diverse self-assembled structures whose stability and interconversion are governed by molecular interactions, composition and external conditions. Understanding these equilibria provides a basis for rationally developing responsive delivery systems, particularly for bioactive molecules.
Recent work will illustrate this progression, combining phase diagrams with DLS/ELS, microscopy (cryo-TEM, cryo-SEM and AFM), DSC, and rheology. Surfactant mixtures provide a starting point: strong non-ideal interactions between oppositely charged surfactants generate rich phase behavior and spontaneous formation of stable vesicles, including systems based on amino-acid-derived amphiphiles.[1] Incorporating photoresponsive chalcone surfactants enables light-induced changes in molecular packing, driving composition-dependent transitions between vesicles, micelles and other nanostructured states, with consequences for drug-release kinetics (Fig. 1).[2,3] Finally, in polymer/surfactant mixtures, coupling surfactant self-assembly with thermoresponsive block copolymers produces intricate temperature-dependent phase transitions and inversely coupled thermogelation.[4] Together, these examples show how perturbing phase equilibria and self-assembly can generate adaptive soft matter for controlled cargo delivery.

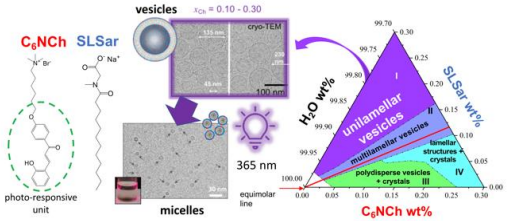
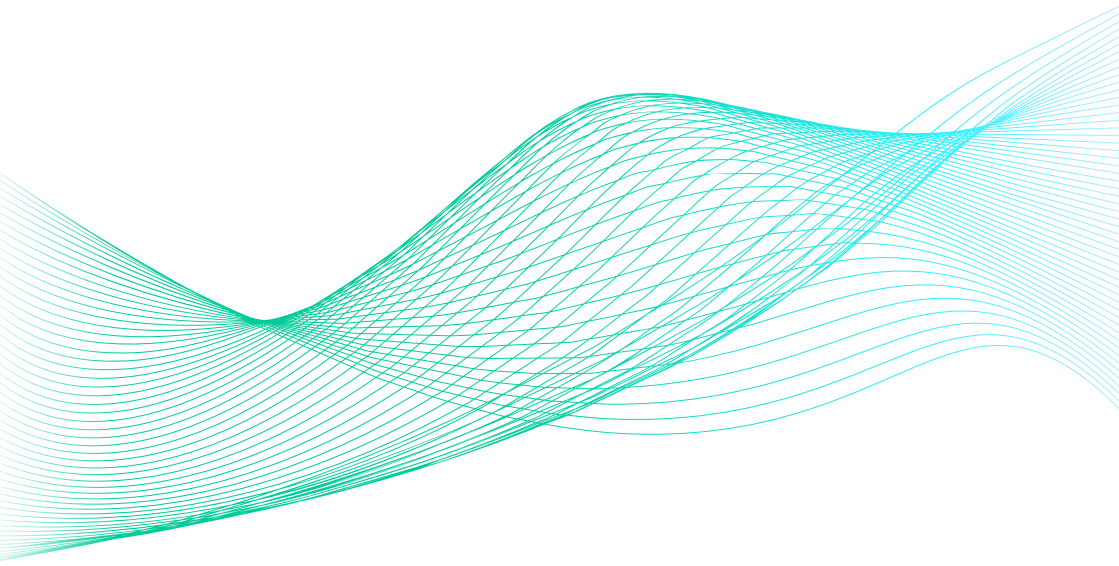


Figure 1: Light-driven vesicle-to-micelle transition in a surfactant mixture.

Acknowledgments
The author gratefully acknowledges all collaborators and FCT for financial support through projects Smart4Vir, MultiDNA, UID/00081/2025 and LA/P/0056/2020.

References
(1) Gonçalves, R.C.F., *et al*. *Nanoscale* 2019, **11**, 5932–5941.
(2) Moreira, D., *et al*. *J. Colloid Interface Sci.* 2023, **650**, 2024–2034.
(3) Moreira, D., *et al*. *J. Mater. Chem. B.* 2026, **14**, 10464–10477.
(4) Machado, R.L., *et al*. *Mater. Today Chem*. 2026, **52**, 103362.

ORAL COMMUNICATIONS



Steering polymorph selection with crystallization additives: lessons from solution and mechanochemical crystallization

A. Bērziņš[a,*], Z. Čerpakovska[a], A. Semjonova[a]
[a] *Faculty of Medicine and Life Sciences, University of Latvia, Jelgavas 1, Riga, Latvia*
[*] *e-mail: agris.berzins@lu.lv*

Controlling which polymorph or solvate crystallizes remains a central challenge in pharmaceutical solid-form development, particularly when concomitant phases or elusive metastable forms limit process robustness. Crystallization additives offer an empirical route to phase control both from solution and via mechanochemical synthesis, yet the mechanisms by which they act as well as criteria for selecting an effective additive remain poorly understood. Her we present examples from additive-controlled solution and mechanochemical crystallization aimed towards understanding the role of the additives and the outcome control mechanism.

Firstly, for nitrofurantoin, several structurally unrelated additives switched the crystallization outcome between polymorphs α and β by reversing their apparent relative solubility, without forming a solid solution or altering the crystal structure, implicating a surface-mediated mechanism rather than a purely kinetic one.[1]

Secondly, for isonicotinamide selected additives enabled reproducible, selective nucleation of otherwise elusive forms,[2] and for 2,6-dimethoxybenzoic acid additives decelerated the SMPT and stabilised the high-temperature form.[3]

Thirdly, for the caffeine-anthranilic acid cocrystal prepared by liquid-assisted grinding, additive and solvent choice jointly governed the crystalline phase obtained. Several liquid amphiphilic additives bearing ether-oxygen- and hydroxyl-rich flexible chains reliably overrode solvent-dependent polymorphism to yield Form II, which could be linked with the Form II's preference to greater reliance on hydrogen bonding.

Across these systems, spanning both solution crystallization and mechanochemical synthesis, additives act through surface-specific interactions, selective inhibition of competing nucleation events, and modulation of phase-transition kinetics. Comparing single-component and cocrystal behaviour across these two preparation routes highlights recurring structure–function patterns in additive selection and points toward a rational, transferable framework for polymorph and cocrystal control in pharmaceutical crystallization.

References

(1) Bērziņš, A., et al. *Cryst. Growth Des.* 2023, **23**, 5469–5476.
(2) Semjonova, A.; Bērziņš, A. *Cryst. Growth Des.* 2023, **23**, 8584–8596.
(3) Semjonova, A.; Bērziņš, A. *Crystals* 2022, **12**, 1161.

Molecular-scale mechanism of γ-pyrazinamide stabilization by urea derivatives

C. Stephan[a,*], G. Gbabode[a], I. B. Rietveld[a], A. Resta[b], A. Ø. Madsen[c]
[a] *University of Rouen Normandy, Rouen, France*
[b] *Synchrotron SOLEIL, Saint Aubin, France*
[c] *University of Copenhagen, Copenhagen, Denmark*
[*] *e-mail: cheng-long.stephan@univ-rouen.fr*

Mastering polymorph selectivity is a key strategy in pharmaceutics, particularly when the pharmaceutically favorable form is thermodynamically metastable. The α-form of pyrazinamide (PZA) is the most common, while the metastable γ-form offers improved solubility but is prone to polymorphic conversion towards a more stable form under ambient conditions.[1]
In this work, we investigate the mechanism by which 1,3-dimethylurea (DMU) selectively stabilizes γ-PZA at a molecular interface. Stacked thin-films were prepared by spin-coating to create a PZA/DMU interface and characterized using analytical and computational tools (see Figure 1).

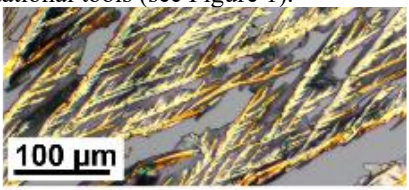


Figure 1: Polarized light microphotography (x10) of a thin film consisting of PZA on DMU.

Grazing-incidence X-ray diffraction unveiled γ-PZA as the dominant phase in the film and resolves its preferred orientation, indicating a specific additive-dependent interfacial mechanism. FT-IR revealed shifts in the PZA C=O and amide bands upon contact with DMU, akin to a H-bonding "capping effect" that selectively blocks the carbonyl required for nucleation and crystal growth of the α-form and other polymorphs. Molecular dynamics simulations of PZA adsorption on a DMU surface identified an edge-on adsorption geometry, stabilized by a dominant (DMU)NH···O=C(PZA) H-bond, strengthening this assumption.

Acknowledgments
Region Normandy, SIXS beamline team at SOLEIL, Cost Action BEST-CSP.

References
(1) Li, K.; Gbabode, G.; Barrio, M.; Tamarit, J.-L.; Vergé-Depré, M.; Robert, B.; Rietveld, I. B. *Int. J. Pharm*. 2020, **580**, 119230.

Unravelling the thermodynamics of lanthanide extraction using hydrophobic eutectic solvents

I. C. M. Vaz[a,*], M. Pinheiro [a], F. Olea [a], M. Bastos[b], L. M. N. B. F. Santos[b], J. A. P. Coutinho[a], N. Schaeffer [a,*]

[a] *CICECO, Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, Portugal*

[b] *CIQUP, Department of Chemistry and Biochemistry, Faculty of Sciences, University of Porto, Portugal*

[*] *e-mail: ines.vaz@ua.pt; nicolas.schaeffer@ua.pt*

The growing societal demand for metals creates urgency in the development of more efficient and sustainable separation processes. Solvent extraction (SX), based on the selective partitioning of ions between two immiscible phases, is the most prevalent technology for metal separation. In this context, hydrophobic eutectic solvents (HES) have emerged as promising alternatives to conventional organic diluents. However, their non-ideal and highly structured nature poses challenges for understanding the factors governing metal transfer.[1] A mechanistic understanding of how solvent composition governs metal extraction is essential to move from trial-and-error towards rational design.

In this work, the solvent extraction of lanthanides is investigated using tri-n-octylphosphine oxide (TOPO) as extractant, incorporated within a HES formed with decanoic acid. The biphasic transfer of trisnitrato complexes of lanthanides ($M(NO_3)_3$) is studied over a range of temperatures, enabling a thermodynamic analysis of the extraction process. Temperature-dependent distribution data are interpreted through a van't Hoff approach to access the overall enthalpic and entropic contributions governing metal partitioning and results are compared with a conventional SX system (TOPO in toluene). To directly quantify the enthalpy of extraction, an isothermal titration calorimetry (ITC) methodology was developed and optimized for HES-based biphasic systems.

The combined van't Hoff and calorimetric analyses provide complementary insights into the energetic landscape of lanthanide extraction in eutectic media, offering a robust basis for understanding the driving forces underlying metal ion partitioning and for designing more efficient and sustainable extraction systems.

Acknowledgments

Funded by the European Union (ERC Starting Grant, DESignSX, project number 101116461). This work was partially developed within the scope of the project CICECO – Aveiro Institute of Materials, UID/50011/2025 & LA/P/0006/2020 (DOI 10.54499/LA/P/0006/2020), financed by national funds through the FCT/MCTES (PIDDAC).

References

(1) Schaeffer, N., et al. *Green Chem.,* 2025, **27**, 4438–4463.

From mixing to phase separation: hydrodynamic insights into cholinium chloride-based ATPS

A. M. S. Jorge[a], J. A. P. Coutinho[b], J. F. B. Pereira[a*]
[a] *CERES, FCTUC, Department of Chemical Engineering, University of Coimbra, Rua Sílvio Lima, Pólo II - Pinhal de Marrocos, 3030-790 Coimbra, Portugal*
[b] *CICECO – Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, Campus Universitário de Santiago, 3810-193 Aveiro, Portugal*
[*] *e-mail:* jfbpereira@eq.uc.pt

Aqueous two-phase systems (ATPS) have gained considerable attention as sustainable liquid–liquid extraction media for the recovery of biomolecules and other high-value compounds. Understanding the dynamics of phase separation is therefore essential for the successful scale-up of ATPS-based extraction processes.

In this work, the phase separation behaviour of three cholinium chloride-based ATPS (PPG400/[Ch]Cl, [Ch]Cl/K_3PO_4, and [Ch]Cl/K_2HPO_4) was investigated by monitoring mixing and settling times at 25 and 50 °C.[1] The results showed that the duration of the mixing step had no measurable effect on the subsequent settling process. Salt/salt ATPS exhibited rapid phase disengagement, reaching equilibrium in less than 150 s, whereas polymer/salt systems required more than 6 h to achieve complete separation. This difference is associated with the stronger salting-out capacity of the inorganic salts, which promotes faster phase formation. Among the properties analysed, the density difference between the coexisting phases was identified as the main parameter governing settling behaviour. Overall, this study provides fundamental insights into the phase separation characteristics of cholinium chloride-based ATPS and defines operating conditions that support their integration into conventional mixer–settler extraction units, facilitating the development of scalable and industrially relevant separation processes.

Acknowledgments
CERES is supported by the Fundação para a Ciência e a Tecnologia (FCT) through the projects UIDB/ EQU/00102/2020 and UIDP/EQU/00102/2020. This work was partly developed within the scope of the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020, financed by national funds through the FCT/MEC (PIDDAC). J.F.B. Pereira and A. M. S. Jorge acknowledge the FCT for funding project HIPERBIOTEX (COMPETE2030-FEDER-00708800) and Fundação Calouste Gulbenkian for funding the project DyeLoop – Circular Technologies for Textile Dyeing.

References
(1) Jorge, A.M.S.; Coutinho, J.A.P.; Pereira, J.F.B. *Sep. Purif. Technol.* 2023, **320**, 124183.
(2) Shahriari, S.; Tomé, L.C.; Araújo, J.M.M.; Rebelo, L.P.N.; Coutinho, J.A.P.; Marrucho, I.M.; Freire, M.G. *RSC Adv.* 2013, **3**, 1835–1843.

Controlling phase equilibria and redox-species partitioning with NaSCN in Ionic-liquid aqueous biphasic electrolytes

G. L. Camilo[a,*], M. L. Alcantara[a], A. M. Ferreira[a], J. A. P. Coutinho[a]
[a] *CICECO – Aveiro Institute of Materials, University of Aveiro, Campus Universitário de Santiago, 3810-193 Aveiro, Portugal*
[*] *e-mail: gcamilo@ua.pt*

Aqueous biphasic systems (ABS) are promising platforms for membrane-free redox flow batteries because thermodynamic phase separation can replace conventional ion-selective membranes while providing two distinct aqueous environments for redox-active species. However, ionic-liquid-based ABS are often limited by narrow liquid-liquid equilibrium regions and salt precipitation. In this work, sodium thiocyanate (NaSCN) was investigated as a formulation strategy to expand the accessible chemical space of ABS composed of $(NH_4)_2SO_4$, chloride-based ionic liquids, and water. NaSCN promotes Cl^-/SCN^- exchange, induces liquid-liquid equilibria in systems otherwise dominated by solid-liquid behavior, and markedly enlarges the liquid-liquid region. The corresponding solid-liquid-liquid precipitation boundary was also determined, defining the effective operational composition window of each system. The broader L-L regions enable formulations with substantially lower ionic-liquid contents, and partial replacement of the ionic liquid by NaSCN was estimated to reduce electrolyte material costs by approximately 21-24%.
Beyond phase formation, NaSCN also modifies solute distribution between the coexisting phases. Methyl viologen partitioning was tuned through NaSCN concentration and ionic-liquid structure, including inversion of phase preference in selected tetraalkylammonium systems. Additional viologen derivatives and $K_4[Fe(CN)_6]$ further demonstrated formulation-dependent selectivity. Cyclic voltammetry showed that electrolyte composition also influences the ferrocyanide oxidation response. Overall, NaSCN provides a simple route to expand the thermodynamic operating window, reduce ionic-liquid demand, and tune both redox partitioning and electrochemical response in ionic-liquid-based ABS.

Acknowledgments
This work was developed within the scope of the CICECO – Aveiro Institute of Materials project UID/50011/2025 (DOI 10.54499/UID/50011/2025) and LA/P/0006/2020 (DOI 10.54499/LA/P/0006/2020), financed by national funds through FCT/MCTES (PIDDAC). The authors acknowledge financial support from the MeBattery project, which received funding from the European Innovation Council of the European Union under Grant Agreement No. 101046742. GLC acknowledges FCT for the Ph.D. grant UI/BD/00343/2024 (DOI 10.54499/2024.00343.BD). AMF acknowledges FCT for the research contract CEECIND/00361/2022 (DOI 10.54499/2022.00361.CEECIND/CP1720/CT0020).

Elesclomol-copper-loaded silk fibroin nanoparticles for glioblastoma therapy

R. Rocha[a,b,*], F. Branco[a,b], M. Mendes[a,b], A. Pais[a], C. Vitorino[a,b]
[a] *CQC- IMS, Department of Chemistry, University of Coimbra, Coimbra, Portugal*
[b] *Faculty of Pharmacy, University of Coimbra, Coimbra, Portugal*
[*] *e-mail: rubenrocha2003@gmail.com*

Glioblastoma (GBM) remains one of the most aggressive and treatment-resistant brain tumors, highlighting the need for novel therapeutic and drug delivery strategies. Elesclomol-copper (ESC^{Cu}) has emerged as a promising anticancer agent associated with copper-dependent cell death mechanisms, but its limited aqueous solubility and stability may restrict its therapeutic application. This study investigated silk fibroin nanoparticles (SNPs) as a delivery platform for ESC^{Cu} (ESC^{Cu}@SNPs), aiming to improve the formulation and explore its therapeutic potential against GBM.

Regenerated silk fibroin (SF) was extracted from *Bombyx mori* cocoons and used to prepare unloaded and ESC^{Cu}@SNPs by antisolvent desolvation. The nanoparticles were characterized in terms of particle size, polydispersity index (PdI), zeta potential, encapsulation efficiency, drug release, secondary protein structure by ATR-FTIR, and thermal behavior by DSC. The biological activity of unloaded and ESC^{Cu}@SNPs was evaluated in human U87 and murine GL261 glioblastoma cells using a resazurin-based metabolic activity assay.

SNPs exhibited particle sizes of approximately 130 nm, PdI values predominantly below 0.20, and a negative zeta potential of approximately -30 mV, with relatively stable colloidal properties during the first 28 days of storage. ESC^{Cu} encapsulation efficiency was approximately 20% and remained stable for at least two weeks, then decreased after four weeks. Importantly, ESC^{Cu} incorporation did not substantially alter the structural organization of the SNPs. Unloaded SNPs were well tolerated by both GBM cell lines, whereas ESC^{Cu}@SNPs induced a marked concentration-dependent reduction in cellular metabolic activity, with a particularly pronounced response in GL261 cells.

Silk fibroin nanoparticles provide a biocompatible and structurally stable platform for ESC^{Cu} delivery, while preserving the antitumour activity associated with ESC^{Cu}. The pronounced response observed in GL261 cells supports further investigation of this formulation in immune-relevant GBM models, including 3D GL261 models and, subsequently, syngeneic immunocompetent systems to explore both antitumor efficacy and potential immune modulation.

Acknowledgments
The Coimbra Chemistry Centre (CQC) is supported by the FCT through the projects UIDB/00313/2025 and UIDP/00313/2025. This works was also funded through the project 2022.06174.PTDC.

Hybrid molecular descriptor-based machine learning for PC-SAFT parameter

P. V. B. Bonjour[a,*], A. M. S. Jorge[a], J. F. B. Pereira[a]
[a] *University of Coimbra, CERES, Department of Chemical Engineering, 3030-790 Coimbra, Portugal.*
[*] *e-mail: bonjour.engqui@gmail.com*

The Perturbed-Chain Statistical Associating Fluid Theory (PC-SAFT) equation of state is widely used to model the thermodynamic behavior of pure compounds and mixtures.[1] Its predictive capability depends on accurate pure-component parameters obtained by regression to experimental thermophysical data. This process is time-consuming and limits the application of PC-SAFT to compounds with sufficient experimental information.[2]

The proposed methodology combines quantum chemistry-derived descriptors obtained from COSMO-RS, including the molecular σ-profile and complementary molecular descriptors, with structural and physicochemical descriptors calculated using RDKit, reducing the need for conventional parameter fitting.

Together, these descriptors provide a representation of molecular size, shape, polarity, hydrogen-bonding capability. Supervised machine learning models are developed to predict the principal PC-SAFT parameters, including the segment number (m), segment diameter (σ), and dispersion energy parameter (ε/k) and further the assessment of their ability to reproduce experimental thermodynamic properties through PC-SAFT calculations.

The proposed framework integrates quantum chemistry, cheminformatics, and thermodynamic modeling to rapidly estimate PC-SAFT parameters, supporting molecular screening and process design.

Acknowledgments
CERES acknowledges financial support from FCT through the projects UID/00102/2025 (https://doi.org/10.54499/UID/00102/2025), UID/PRR/00102/2025 under the Recovery and Resilience Programme (PRR) of the Portuguese Republic (https://doi.org/10.54499/UID/PRR/00102/2025) and Equipar+2 (https://doi.org/10.54499/UID/PRR2/00102/2025).

References
(1) Gross, J.; Sadowski, G. *Ind. Eng. Chem. Res*. 2001, **40**, 1244–1260.
(2) Hans, H.; Schmitt, S.; Jirasek, F. *Curr. Opin. Chem. Eng*. 2026, **51**, 101236.

AI-enabled discovery of deep eutectic solvents and their chemical space

J. P. Santos[a], F. H. B. Sosa[a], D. O. Abranches[a], J. A. P. Coutinho[a]
[a] *CICECO—Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal*
[*] *e-mail: jdinis@ua.pt*

Deep eutectic solvents (DESs), binary liquid mixtures noted for their strong intermolecular interactions, have emerged as promising green alternatives to traditional organic solvents. The design of these novel solvents is complex, as their properties do not simply reflect the weighted average of their precursors. Incorporating low molecular weight compounds, such as water, to reduce viscosity or modulate other properties is a common practice. This leads to an overly complex and extensive DES design space, where the number, chemical nature, and relative composition of precursors must be carefully tuned. Machine learning (ML), with its innate ability to correlate variables, presents a promising alternative to trial-and-error approaches in the design of DESs.

In this work, Gaussian processes (GPs) were used to fit and predict several physicochemical properties of DESs, namely density, viscosity, and melting temperature. Experimental data was collected from the literature, including over 400 unique DES combinations and more than 4000 independent data points. Each dataset was carefully split into training, validation, and testing sets to determine the optimal GP architecture and hyperparameters for each physicochemical property. Coefficients of determination exceeding 0.95 were achieved for all studied properties, including viscosity, which spanned values over eight orders of magnitude, and melting temperature, which encompassed a range of nearly 700 K. Using the trained GP models, new DES-based lubricants were designed by exploring the sigma profile space of DESs. The GPs suggested novel combinations of precursors not present in the original database to achieve desired viscosities and melting temperatures. These novel DESs were experimentally prepared and characterized for the first time in this work. Viscosity and tribological properties were also measured, which surpassed common standards in the literature for low and high operational temperatures, effectively leading to DES formulations suitable for lubricant applications.

Acknowledgments
This work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UID/50011/2025 (DOI 10.54499/UID/50011/2025) & LA/P/0006/2020 (DOI 10.54499/LA/P/0006/2020), financed by national funds through the FCT/MCTES (PIDDAC). Filipe Sosa acknowledges FCT (CEECIND/07209/2022).

Structural investigation of the polymorphic transition of 1,3-dimethylurea

G. Gbabode[a], M. Sulli[a,b]
[a] *Univ Rouen Normandie, Normandie Univ, SMS , UR 3233, F-76000 Rouen, France*
[b] *Università degli Studi di Firenze, Piazza San Marco 4, 50121 Firenze, Italy*
[*] *e-mail: gabin.gbabode@univ-rouen.fr*

1,3-dimethylurea (called hereafter DEU) is a small organic molecule that attracted our attention as it has been shown to favor the crystallization of the metastable gamma form of pyrazinamide (a common drug used in the treatment of tuberculosis[1]) when it is present in solution with pyrazinamide.[2] Namely, the gamma form converts back to stable alpha form within weeks in the absence of DEU while it can be maintained over a year when DEU is present (ongoing work). However, no crystal structure has been reported for DEU that might help to understand this phenomenon.

In this contribution, we will present our results on the investigation of the polymorphic behaviour of DEU and on the crystal structure determination of 2 polymorphs (named forms I and II) of DEU from synchrotron X-ray powder diffraction data. Noticeably, this work combines computational (DFT) and experimental (X-ray powder diffraction, DSC, solid state NMR, Second Harmonic Generation -SHG-) techniques to achieve the most accurate crystal structure possible for each polymorph. From those results, a hypothesis of transition mechanism is proposed for the enantiotropic transition between forms I and II occurring upon heating.

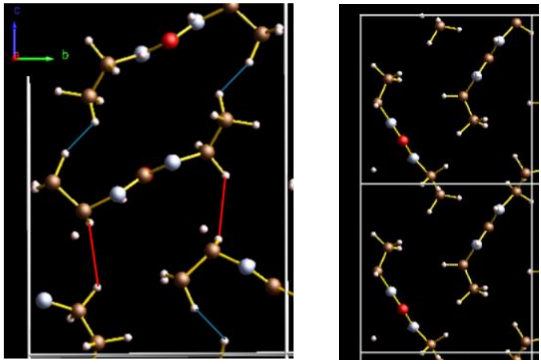


Figure 1: Representations in the (b, c) plane of the crystal structure of forms (left) I and (right) II.

References

(1) Zhang, Y.; Mitchison, D. *Int. J. Tuberc. Lung Dis.* 2003, **7**, 6–21.
(2) Li, K. *Research thesis,* University of Rouen Normandie, Rouen, 2021.

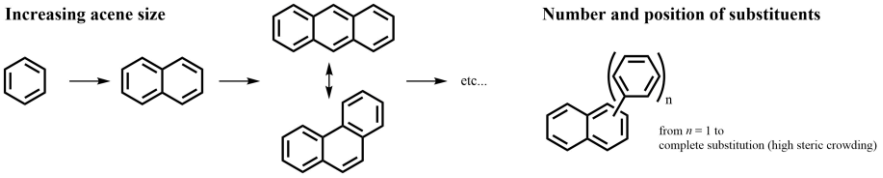
Thermodynamics of phase behavior and polymorphism in phenylacenes

C. F. R. A. C. Lima*, C. S. T. Pinto, F. V. Ribeiro, L. M. N. B. F. Santos, J. C. S. Costa

CIQUP, *Institute of Molecular Sciences (*IMS*),*
Department of Chemistry and Biochemistry, Faculty of Science, University of Porto,
Rua do Campo Alegre, 4169-007 Porto, Portugal
**e-mail: carlos.lima@up.pt*

This work presents a systematic thermodynamic assessment of phase behavior in a family of phenylacenes, including phenyl-substituted derivatives of benzene, naphthalene, anthracene and larger acenes. Experimental thermodynamic measurements include Differential Scanning Calorimetry (DSC) studies of solid-solid transitions and fusion, together with sublimation measurements using both calorimetric and Knudsen effusion methodologies. The observed trends will be analysed in terms of the corresponding enthalpy and entropy changes of phase transitions, with particular emphasis on their implications for phase stability, intermolecular packing and polymorphism. Whenever possible, the thermodynamic results will be complemented by structural information from X-ray diffraction and optical microscopy.

The selected families of compounds were designed to investigate the effects of: (i) molecular isomerism (e.g., comparisons among phenylnaphthalenes and between phenylanthracenes and phenylphenanthrenes); (ii) acene size (benzene → naphthalene → anthracene); (iii) the number and position of phenyl substituents; and (iv) increasing steric crowding (including the cases of hexaphenylbenzene, octaphenylnaphthalene, decaphenylanthracene. Overall, the study aims to establish relationships between molecular structure, intermolecular interactions, crystal packing and thermodynamic stability, providing insight into the molecular factors governing phase behavior and polymorphism in representative aromatic systems.



Acknowledgments
The authors thank to the Portuguese Foundation for Science and Technology (FCT) for financial support to CIQUP, Faculty of Science, University of Porto (Project UID/PRR/00081/2025, DOI https://doi.org/10.54499/UID/PRR/00081/2025), and IMS – Institute of Molecular Sciences (LA/P/0056/2020), Faculty of Science, University of Porto.

Solid-state diversity in bisphenolic compounds: the roles of molecular flexibility and hydrogen bonding in polymorphism and solvation

J. A. Baptista[a,*], R. A. E. Castro[a,b], E. Fantechi[c], L. Chelazzi[c], S. Ciattini[c], M. T. S. Rosado[a], M. E. S. Eusébio[a]

[a] *University of Coimbra, CQC/IMS, Department of Chemistry, Coimbra, Portugal;*
[b] *University of Coimbra, Faculty of Pharmacy, Coimbra, Portugal*
[c] *Università degli Studi di Firenze Centro di Cristallografia Strutturale, Firenze, Italy*
**e-mail: jabaptista@qui.uc.pt*

In this work, we investigate the solid-state landscapes of three structurally related bisphenolic compounds: the antihyperlipidaemic drug probucol (PROB), tetramethyl bisphenol A (TM-BPA), and 4,4′-methylenebis(2,6-di-tert-butylphenol) (TB-BPF). PROB is a highly flexible molecule and, although it contains two hydroxyl groups, their accessibility for intermolecular interactions is significantly hindered by neighboring tert-butyl substituents. In contrast, TM-BPA and TB-BPF possess lower conformational flexibility, while the hydroxyl groups of TM-BPA are substantially more accessible for hydrogen-bond formation.

The influence of crystallization conditions, including solvent selection, on polymorph and solvate formation was systematically examined for all three compounds. Comparative polymorph and solvate screening of these three compounds was undertaken to elucidate the molecular characteristics that govern the formation of polymorphic and solvated forms within this family of bisphenolic compounds.

The results demonstrate that molecular flexibility and hydrogen-bonding capacity are the primary factors governing the solid-state landscapes of the three compounds. The substantially richer polymorphic diversity observed for PROB[1], compared with TB-BPF, is attributed to its greater conformational flexibility, which allows access to a broader range of crystal-packing arrangements. In contrast, TM-BPA exhibits a much more limited solid-form landscape.

Solvate formation was also found to depend strongly on solvent properties. Small, low-flexibility hydrogen-bond-acceptor solvents readily formed solvates with both PROB and TB-BPF through relatively weak intermolecular hydrogen-bonding interactions.

Acknowledgments

Coimbra Chemistry Center/Institute of Molecular Sciences (CQC/IMS) is supported by FCT, Foundation for Science and Technology (UIDB/00313/2020, UIDP/00313/2020. Thanks are due to UCQFarma for the use of the PXRD facility. J.A.B. acknowledges FCT for financial support (PhD grant UI/BD/150859/2021).

References

(1) Baptista; J.A., et al. *Cryst. Growth Des.* 2025, **25**, 812–82.

Study of the solid-state landscape of the (an)hydrated forms of $K_7[SbW_6O_{24}]$, a new type of turn-off luminescence humidity sensors.

S. Kissage-Silva[a], L. Papin[b], M. Sanselme[a], N. Couvrat[a], R. Dessapt[b], Y. Cartigny[a*]

[a] *Univ Rouen Normandie, Normandie Univ, SMS, UR 3233, F-76000 Rouen, France.*

[b] *Nantes Université, CNRS, Institut des Matériaux de Nantes Jean Rouxel, IMN,F-44000, Nantes, France*

[*] *e-mail: yohann.cartigny@univ-rouen.fr*

A new type of turn-off photoluminescence (PL) humidity sensor based on a water-responsive anhydrous alkali lanthanide-free $[SbW_6O_{24}]^{7-}$ polyoxometalate (POM) was reported by our consortium. Na7[SbW6O24] was recently obtained by heating its parent hydrate $Na_7[SbW_6O_{24}]$,16H_2O at 200°C. Upon exposure to a moisture-laden atmosphere at room temperature, the anhydrous phase converted back to the hydrated one, leading to a complete quenching of the intense PL intensity.

A similar behavior was also reported for an another compound in this family of materials: the compound $K_7[SbW_6O_{24}]$, 6H_2O. The present work investigates the dehydration/rehydration processes of these materials in order to investigate the effect of the hydration level of the solid on the photoluminescent properties.

The experimental investigations were conducted by a combination of powder X-ray diffraction (powder and Single crystals analyses) under variable temperature or humidity, optical microscopy, thermal analyses, and dynamic vapor sorption (DVS).

This lead to highlight the solid-state landscape of these systems by characterizing all the hydrated forms and their relationship vs temperature or humidity variations.

Acknowledgments

Authors thanks the French ANR program for funding the ALPS-WATER project (2024–2028).

References

(1) Bagghi, A.; Deniard, P.; Cartigny, Y.; Dessapt, R. *J. Mater. Chem. C* 2024, **12**, 1474–1484.

Thermal and chemical stability of ionic liquids under high-temperature conditions

J. Fabian[a,*], M. L. Alcantara[a], C. F. H. B. Sosa[a], J. A. P. Coutinho[a]
[a] *CICECO – Aveiro Institute of Materials, University of Aveiro, Campus Universitário de Santiago, 3810-193 Aveiro, Portugal*
[*] *e-mail: joaofabian@ua.pt*

Ionic liquids (ILs) are increasingly considered as enabling solvents for intensified high-temperature processes, including CO_2 hydrogenation to methanol and gas dehydration. Their tunable physicochemical properties can improve product removal and separation in CO_2 hydrogenation, preferential absorption of methanol and water can shift the reaction equilibrium and promote higher methanol yields.[1] Nevertheless, their applicability ultimately depends on their ability to withstand prolonged thermal and chemical exposure.

IL stability is commonly assessed using the onset decomposition temperature obtained from short, dynamic thermogravimetric analysis (TGA). However, this parameter may not represent long-term operating limits and can overestimate practical stability by 100-300 °C.[2] To address this limitation, we evaluate the temperature associated with 1% mass loss after 10 h as a more representative descriptor of long-term thermal stability. Instead of the 5-7 TGA experiments typically reported for its determination, we investigated a reduced burden methodology with a dynamic TGA and only 1 isothermal TGA.

Chemical stability is also essential because ILs may interact with reaction products, catalysts, and reactor materials during operations at high temperatures. Selected ILs were therefore exposed to conditions representative of CO_2 hydrogenation to methanol at 240 °C, and possible degradation was investigated by ^{1}H and ^{13}C NMR spectroscopy. The combined approach provides practical criteria for assessing IL durability while reducing the effort required to identify suitable candidates for prolonged high-temperature operation.

Acknowledgments
This work was developed within the scope of the project CICECO Aveiro Institute of Materia ls, UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020, financed by national funds through the FCT/MCTES (PIDDAC). This study also received financial support from Illimited project, financed by Horizon Europe agreement n°101192964. Filipe H. B. Sosa acknowledges FCT (CEECIND/07209/2022)

References
(1) Reichert, J.; Maerten, S.; Meltzer, K.; Tremel, A.; Baldauf, M.; Wasserscheid, P.; Albert, J. *Sustain. Energy Fuels* 2019, **3**, 3399–3405.
(2) Cao, Y.; Mu, T. *Ind. Eng. Chem. Res*. 2014, **53**, 8651–8664.

Molecular basis of trehalose-induced stabilization of phase coexistence in mixed phospholipid bilayers

A. M. Alves[a,b], M. J. Moreno[a,b,*], L. M. S. Loura[a,c]
[a] *Coimbra Chemistry Center, Institute of Molecular Sciences (CQC-IMS), University of Coimbra, 3004-535 Coimbra, Portugal;*
[b] *Department of Chemistry, Faculty of Sciences and Technology, University of Coimbra, 3004-535 Coimbra, Portugal;*
[c] *Faculty of Pharmacy, University of Coimbra, 3000-548 Coimbra, Portugal*
[*] *e-mail: mmoreno@ci.uc.pt*

Trehalose is widely employed as a membrane protectant, yet the molecular mechanisms underlying its e ects on membrane organization remain incompletely understood. Here, fluorescence spectroscopy and all-atom molecular dynamics (MD) simulations were combined to investigate the influence of trehalose on the phase behavior of mixed DMPC:DSPC lipid bilayers. Fluorescence anisotropy measurements showed that 1 M trehalose lowers the onset and raises the completion temperature of the main phase transition, broadening the gel-fluid coexistence region. Consistent with these observations, MD simulations revealed progressive disordering of the gel phase before the transition, whereas the average bilayer structural properties were only minimally a ected. Trehalose exhibited a modest enrichment at the membrane interface, where it formed hydrogen-bond bridges between neighboring lipid phosphate groups. These bridges occurred preferentially between the more exposed DSPC molecules, promoting lateral segregation into DSPC-rich domains. Together, the experimental and computational results indicate that trehalose modulates membrane phase behavior primarily through selective interactions with DSPC lipids rather than by substantially perturbing the overall bilayer structure. These findings provide a molecular basis for the trehalose-induced stabilization of gel-fluid phase coexistence in mixed phospholipid membranes.

Predicting partitioning of biomolecules in aqueous biphasic systems

M. D. Pinhão[a,*], E. V. Capela[a], J. A. P. Coutinho[a], M. G. Freire[a], D. O. Abranches[a]

[a] *CICECO-Aveiro Institute of Materials, University of Aveiro, Portugal*
[*] *e-mail: margaridapinhao@ua.pt*

Aqueous Biphasic Systems (ABSs) have emerged as a viable approach in the purification of biomolecules without loss of biological activity. Unlike traditional water-organic biphasic systems, ABSs consist of two immiscible aqueous phases and are non-toxic, non-flammable, and biocompatible. Ionic liquids (ILs) are often used as ABS constituents to better control biomolecule-solvent interactions and enhance separation performance. However, given the vast library of ILs, the selection of suitable systems for each target biomolecule relies on laborious trial-and-error campaigns. Machine learning (ML), particularly Gaussian process (GP) models have been shown to be capable of predicting physicochemical properties of materials and emerge as a viable alternative to help design IL- based ABSs. In this work, GP models were developed to predict the partitioning behaviour of several biomolecules, such as caffeine, nicotine, phenylalanine, gallic acid and levodopa, in different polyethylene glycol-dextran (PEG-DEX) ABSs. Sigma profiles, molecular descriptors derived from quantum chemistry calculations, were employed. The GP models were able to predict the partition coefficients of all biomolecules across several different ABSs. Overall, coefficients of determination of 0.99 and 0.85 were attained for the training and testing sets, respectively. The testing set consisted of novel ABSs never seen before by the model, highlighting its predictive and generalization capability. The methodology developed in this work significantly accelerates the design of separation and purification processes based on ABSs, guiding the experimental design and reducing trial and error screening.

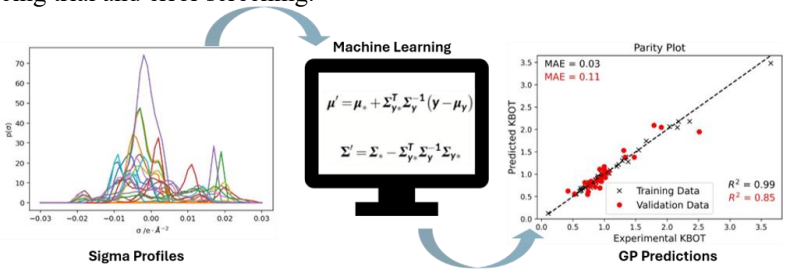


Figure 1: Sigma profiles of all the Ionic Liquids added as adjuvants to the Aqueous Biphasic Systems, used as input to the Gaussian Process model to predict the Partition Coefficients of the solutes in the DEX-rich phase.

Understanding the molecular interactions governing PEG/PPG Aqueous two-phase system formation

A. M. S. Jorge[a,*], G. M. C. Silva[b], J. A. P. Coutinho[b], J. F. B. Pereira[a]
[a] *CERES, FCTUC, Department of Chemical Engineering, University of Coimbra, Rua Sílvio Lima, Pólo II - Pinhal de Marrocos, 3030-790 Coimbra, Portugal*
[b] *CICECO – Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, Campus Universitário de Santiago, 3810-193 Aveiro*
[*] *e-mail: alexandrej@eq.uc.pt*

Polymer/polymer ATPS have been extensively investigated for the separation,extraction, and purification of biomolecules and other high-value compounds.[1,2]
Despite decades of research, the molecular interactions governing phase separationin polymer/polymer ATPS remain incompletely understood. To address this
knowledge gap, we investigated the molecular interactions in ternary mixtures composed of polyethylene glycol (PEG600), polypropylene glycol (PPG400), and water. Molecular dynamics (MD) simulations were performed to characterize polymer–polymer and polymer–water interactions over a range of temperatures and water concentrations. In parallel, the Conductor-like Screening Model for Realistic Solvents (COSMO-RS) was employed to evaluate the thermodynamic properties of the polymer–water binary mixtures and to investigate their relationship with ATPS formation.. Overall, the results identify polymer–water interactions as the primary driving force governing phase separation in this system.

Acknowledgments
CERES is supported by the Fundação para a Ciência e a Tecnologia (FCT) through the projects UIDB/ EQU/00102/2020 and UIDP/EQU/00102/2020. This work was partly developed within the scope of the project CICECO-Aveiro Institute of Materials, UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020, financed by national funds through the FCT/MEC (PIDDAC). J.F.B. Pereira and A. M. S. Jorge acknowledge the FCT for funding project HIPERBIOTEX (COMPETE2030- FEDER-00708800) and Fundação Calouste Gulbenkian for funding the project DyeLoop – Circular Technologies for Textile Dyeing.

References
(1) Asenjo, J.A.; Andrews, B. A. *J. Chromatogr. A* 2011, **1218**, 8826–8835.
(2) Ferreira, A.M.; Passos, H.; Okafuji, A.; Tavares, A.P.M.; Ohno, H.; Freire, M.G.; Coutinho, J.A.P. *Green Chem*. 2018, **20**, 1218–1223.

What's the best predictive model for ionic liquid screening? COSMO-SAC, COSMO-RS and GNN

M. L. Alcantara[a,*], E. T. Souza Jr.[b], J. G. Rittig[c], R. de P. Soares[b], P. B. Staudt[b], P. Schwaller[c], J. A. P. Coutinho[a]

[a] *CICECO, University of Aveiro, 3810-193 Aveiro, Portugal*
[b] *LVPP, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil*
[c] *LIAC, EPFL, Lausanne, Switzerland*
**e-mail: murilo.la@ua.pt*

Screening ionic liquids (ILs) is a ranking problem before it is a prediction problem: among millions of cation–anion combinations, what matters is which candidates reach the laboratory, not the value assigned to each. Models are nevertheless compared almost exclusively on absolute error. We benchmark six physics-based variants and one data-driven model against ~55,000 experimental infinite-dilution activity coefficients (γ^{∞}) in ILs, mostly imidazolium-based with hydrocarbon solutes. The physics-based set is COSMO-RS (COSMOtherm 2025) and COSMO-SAC (JCOSMO 3.1) with def-BP-TZVP and def2-BP-TZVPD parameterisations; 1–3 the data-driven model is a temperature-dependent graph neural network (GNN) on molecular graphs.4 All are evaluated on the same database with MAE and RMSE in ln $\gamma\infty$, R^2, and the Spearman rank correlation ρ, which governs screening.

COSMO models predict activity coefficients qualitatively well but with large quantitative deviations in IL systems, regardless of model or level of theory; raising the level from TZVP to TZVPD-FINE unexpectedly increased COSMO-RS deviations. COSMO-SAC 25 and COSMO-RS (TZVP) presented the lowest deviations among COSMO models. The main difference is cost: 55k γ^{∞} took <2 min in JCOSMO versus about a day in COSMOtherm 2025 — three orders of magnitude. The GNN[1] is far more accurate and ranks better still (ρ = 0.98 and 0.97) within its training domain, but degrades outside it, where no thermodynamic constraint applies. The result is a division of labour, not a winner: the GNN ranks in-domain at negligible cost, while COSMO gives physically constrained extrapolation to unseen chemistries. Within ILIMITED, it ranked a 19.5 M IL space for in-situ methanol/water sorption at 240 °C, and the best candidates are indeed in agreement with the experimental evaluation of literature data.

Acknowledgments

Developed within CICECO – Aveiro Institute of Materials (UIDB/50011/2020, UIDP/50011/2020, LA/P/0006/2020), financed by national funds through FCT/MCTES (PIDDAC), and funded by the European Union, ILIMITED project, Grant Agreement No 101192964.

References

(1) Rittig, J. G., et al. *Comput. Chem. Eng.* 2023, **171**, 108153.

From molecular structure to environmental mobility: predicting key properties of substituted benzenes

B. Pinheiro*, A. Almeida, M. Monte

Research Centre in Chemistry of University of Porto (CIQUP), Institute of Molecular Sciences (IMS), Department of Chemistry and Biochemistry, Faculty of Sciences, University of Porto, Rua do Campo Alegre, P-4169-007 Porto, Portugal

* *e-mail: bruno.pinheiro@fc.up.pt*

Developing accurate, robust, and user-friendly methods for estimating thermodynamic properties is essential for understanding environmental mobility - specifically how compounds behave, distribute, and transform in the environment. This understanding is critical for effective environmental protection, pollution management, and informed regulatory decision-making. A previously proposed approach estimated the sublimation vapor pressures (Gibbs energies) and enthalpies of substituted benzenes using a database of around 240 benzene derivatives with 30 different substituents. The prediction equations accounted for the contributions of substituent groups for the sublimation properties, fusion temperature, and interactions between groups in ortho and para positions. Although the method was later extended to other thermodynamic properties, only the Gibbs energies of vaporization were accurately predicted across the full range of substituents. The study subsequently focused on halogenated benzenes, proposing simple and effective equations for key properties relevant to environmental mobility, including water solubility at 25 °C, Gibbs energies of hydration, vaporization and sublimation, fusion temperatures, Henry's law constants, and octanol/water partition coefficients. In this study, updates to the database are presented, incorporating new experimental data for substituted benzenes containing both non-ionizable functional groups and halogen atoms, alongside improved estimation equations for predicting these properties.

Acknowledgments

This work was supported by the Fundacão para a Ciência e Tecnologia (FCT) (funded by national funds through the FCT/MCTES (PIDDAC)) to CIQUP, Faculty of Sciences, University of Porto (Project UIDB/00081/2020) and IMS - Institute of Molecular Sciences (LA/P/0056/2020)). B. Pinheiro thanks FCT for the award of a PhD research grant (UI/BD/152715/2022).

References

(1) Monte, M.J.S.; Almeida, A.R.R.P. *Struct. Chem*. 2013, **24**, 2001–2016.

(2) Monte, M.J.S.; Almeida, A.R.R.P. *Chemosphere* 2017, **189**, 590–598.

Crystal structure and behavior of the cocrystal salt (±)Ibuprofen$_2$HK

E. Collet Salvet[a,b,*], M. Sanselme[a], Y. Cartigny[a], R. Texeira[b], C. Rougeot[b], G. Coquerel[a]

[a] *Univ Rouen Normandie, Normandie Univ, FR3038, SMS, UR 3233, F-76000 Rouen, France*

[b] *Sanofi, Analytical Characterization Laboratories, 371 rue du Pr. Joseph Blayac- 34184 Montpellier, France*

[*] *e-mail: elisa.collet@univ-rouen.fr*

Solid-state form selection (salts, co-crystals, polymorphs…) is a key step to optimize phase stability and physicochemical behavior of active pharmaceutical ingredients[1]. Yet, the link between the intermolecular interactions defining a given crystal structure and the resulting equilibrium behavior is rarely established.

This connection is studied here in the ibuprofen–potassium system, through the 2:1 cocrystal salt (±)Ibu$_2$HK and the equimolar salt (±)IbuK. The structure of (±)Ibu$_2$HK, solved by single-crystal X-ray diffraction, reveals an alternation of two layers: one in which potassium cations bridge carboxyl–carboxylate pairs associated through two short O···O contacts (2.437 and 2.447 Å), each with a shared hydrogen atom, and one formed by the isobutyl groups of ibuprofen (see Figure 1). Ionic, hydrogen-bonding and dispersive interactions therefore coexist within the single crystal.

Each interaction can influence the behaviors of the crystal and its responses to the environment. For example (±)Ibu$_2$HK shows negligible moisture uptake (<0.5%, 0–90% RH) and is destroyed in a minute in liquid water, while the deliquescent (±)IbuK behaves oppositely. To date it seems difficult to anticipate the contrast between the behaviors of these solid phases by simply knowing their structural features.

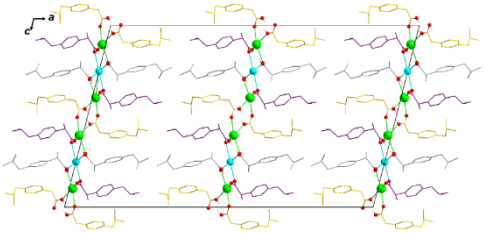


Figure 1 Projection along b axis of the crystal packing.

References

(1) Byrn, S.R.; Henck, J.-O. *Drug Discov. Today Technol.* 2012, **9**, e73–e78.

Effect of alkyl chain length on thermophysical properties of 2-ethoxyethanol + alcohol mixtures

K. Samadi[a,b,*], M. Lifi[c], N. Muñoz-Rujas[b], F. Aguilar[b], F. E. M'hamdi Alaoui[a]

[a] *Energy Laboratory, Faculty of Sciences, University of Abdelmalek Essaadi, Tetouan, Morocco*

[b] *Departamento de Ingeniería Electromecánica, Escuela Politécnica Superior, Universidad de Burgos, Spain, Burgos*

[c] *Department of Mathematics and Computing, Faculty of Science, University of Burgos, Spain, Burgos*

[*] *e-mail: ksx1021@alu.ubu.es*

The thermophysical behavior of binary mixtures containing glycol ethers and higher alcohols is important for understanding molecular interactions in oxygenated systems. In this work, three binary mixtures, namely 2-ethoxyethanol + 1-butanol, 2-ethoxyethanol + 1-hexanol, and 2-ethoxyethanol + 1-heptanol, were studied over the entire composition range at temperatures of 293.15, 303.15, 313.15, and 323.15 K and atmospheric pressure. Density (ρ), speed of sound (u), and refractive index (n_d) were measured, and the corresponding excess molar volume (V^E), isentropic compressibility (κ_s), and refractive index deviation (Δn_d) were derived.

The results show positive V^E values for all systems, indicating expansion upon mixing and the predominance of dispersive interactions. The Δn_d values are negative for mixtures containing 1-butanol and 1-hexanol, and positive for the 1-heptanol system, reflecting differences in molecular packing and intermolecular interactions. The κ_s values exhibit composition-dependent variations, supporting structural changes within the mixtures. The derived properties were successfully correlated using Redlich–Kister polynomial expansions, yielding excellent agreement with experimental data. These results provide insight into the effect of alcohol chain length on the thermophysical behavior of glycol ether–alcohol mixtures.

Acknowledgments

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

(1) Samadi, K.; Lifi, M.; Lifi, H.; Ouakarrouch, M.; Aguilar, F.; Alaoui, F.E.M. *Thermochim. Acta* 2026, **759**, 180259.

Fractionation of winter savory essential oil model mixtures using imidazolium-based ionic liquids

A. Zambom[a,b,c,*], O. Ferreira[b], J. A. P. Coutinho[c], S. P. Pinho[b], S. M. Vilas-Boas[a], H. Rodríguez[a]

[a] *CRETUS, Department of Chemical Engineering, Universidade de Santiago de Compostela, Santiago de Compostela, Spain*

[b] *CIMO, LA SusTEC, Instituto Politécnico de Bragança, Campus de Santa Apolónia, Bragança, Portugal*

[c] *CICECO, Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, Aveiro, Portugal* * *e-mail: aline.z@ua.pt*

Plant-derived essential oils (EOs) are predominantly composed of monoterpenes and monoterpenoids (> 90%) with high potential value for industrial applications if adequately fractionated. To date, research on EO fractionation has focused on citrus and pine species, underdeveloping efficient strategies for purifying EO components from other species. To expand knowledge in this field, this study explores imidazolium-based ionic liquids (ILs) as separation agents for the fractionation of winter savory EO, using carvacrol, *p*-cymene, and γ-terpinene as representative compounds in a model oil mixture.[1] Initially, liquid-liquid equilibrium (LLE) measurements were carried out for five ternary systems (*p*-cymene + carvacrol + IL) at 298.2 K and 318.2 K, evaluating ILs formed by pairing the 1-ethyl-3-methylimidazolium cation ($[C_2mim]^+$) with the acetate ($[OAc]^-$), propionate, diethylphosphate, dicyanamide ($[DCA]^-$), or thiocyanate anions. The ILs showing the best separation efficiency were $[C_2mim][OAc]$ and $[C_2mim][DCA]$, with solute distribution ratios up to 24.8 and selectivities up to 240. These two ILs were selected to measure the corresponding ternary systems (*p*-cymene + γ-terpinene + IL) and (carvacrol + γ-terpinene + IL), thereby completing the LLE measurements of all ternary subsystems of the quaternary system (*p*-cymene + γ-terpinene + carvacrol + IL). The joint correlation of the measured LLE data using the NRTL model yields a set of binary interaction parameters that enable a reliable thermodynamic description of the phase diagrams, supporting, for example, the simulation of liquid-liquid extractors for targeted fractionation.

Acknowledgments

The authors acknowledge financial support from the Spanish Ministry of Science and Innovation through project TED2021-131784B-I00, and the Portuguese Foundation for Science and Technology (FCT/MCTES) through UIDB/00690/2020, UIDP/00690/2020, LA/P/0007/2020, and CICECO-Aveiro Institute of Materials (UIDB/50011/2020, UIDP/50011/2020 and LA/P/0006/2020). A. Zambom acknowledges FCT for her Ph.D. grant UI/BD/154740/2023. S. M. Vilas-Boas acknowledges the Spanish Ministry of Science, Innovation and Universities for the Juan de la Cierva grant (JDC2023-051385-I).

References

(1) Navarro-Rocha, J., et al. *Ind. Crops Prod. 2020,* **145**, 111958.

Solubility and solid-state behavior of metacetamol and paracetamol in pure and mixed solvents

M. A. R. Martins[a,*], A. Zambom[a,b], L. G. Arantes[a], P. Brandão[b], J. A. P. Coutinho[b], O. Ferreira[a], S. P. Pinho[a]

[a] *CIMO, LA SusTEC, Instituto Politécnico de Bragança, Campus de Santa Apolónia, 5300-253 Bragança, Portugal*

[b] *CICECO − Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, 3810193 Aveiro, Portugal*

[*] *e-mail: moniamartins@ipb.pt*

The study of drug solubility in different solvents, as well as their thermal behavior and crystalline structure, plays a crucial role in pharmaceutical development. This work investigates the physicochemical properties of metacetamol and paracetamol, two structural isomers with distinct levels of scientific attention.[1,2]

For metacetamol, solubility was determined in pure and mixed solvents over the temperature range of 298.15 to 323.15 K using the gravimetric method. Complementary studies on paracetamol evaluated its solubility in aqueous solutions containing representative organic solvents, ionic liquids, and salts, providing a systematic comparison of solvent effects on drug dissolution. The combined experimental data were further interpreted using the COSMO-RS model, providing molecular-level insights into solvent-solute interactions and the mechanisms governing solubility enhancement. The solid phases in equilibrium were characterized by PXRD and NMR to investigate possible polymorphism and assess stability. For metacetamol, DSC and TGA were also performed to determine the melting behavior, thermal stability, and enthalpies of the two solid phases.

Overall, these results provide new thermodynamic, thermal, and solid-state data for two pharmaceutically relevant compounds and contribute to a better understanding of solvent effects on drug solubility and stability.

Acknowledgments

This work was supported by national funds through FCT/MCTES (PIDDAC): CIMO UID/00690/2025 (10.54499/UID/00690/2025) and UID/PRR/00690/2025 (10.54499/UID/PRR/00690/2025); SusTEC, LA/P/0007/2020 (DOI: 10.54499/LA/P/0007/2020), and project CICECO–Aveiro Institute of Materials, UID/50011/ 2025 (DOI 10.54499/UID/50011/2025) & LA/P/0006/2020 (DOI 10.5 4499/LA/P/0006/2020).

References

(1) Natarajan, A.; Karuppannan, S. *J. Cryst. Growth* 2025, **654**, 128078.

(2) Zambom, A.; Santos, J.; Brandão, P.; Gaschi, P.S.; Martins, M.A.R.; Coutinho, J.A.P.; Ferreira, O.; Pinho, S.P. *under revision in J. Pharm. Sci*.

Effect of water in the solubility of phenolics acids in diol-based eutectic solvents

B. C. Jesus [a,b,c,*], I. M. Marrucho[a], N. Galamba[b], M. Miquel-Gonzalez[c], C. A. Martins[d]

[a] *CQE - Centro de Química Estrutural and IMS - Institute of Molecular Sciences, DEQ, Instituto Superior Técnico, ULisboa, Lisboa, Portugal*

[b] *Biosystems and Integrative Sciences Institute, Faculdade de Ciências, ULisboa, Lisboa, Portugal*

[c] *Dep. de Ingeniería Química Industrial y del Medio ambiente, ETS Ingenieros Industriales, UPMadrid, Madrid, Spain*

[d] *MARE - Marine and Environmental Sciences Centre and ARNET – Aquatic Research Network, ULO, Leiria, Portugal*

[*] *e-mail: barbaracmjesus@tecnico.ulisboa.pt*

Eutectic solvents (ES) are promising alternatives for extracting phenolic compounds (PCs) from natural matrices due to their ability to enhance PCs solubility [(1)]. However, the mechanisms behind this effect, particularly the role of water in modulating ES structure and intermolecular interactions, remain poorly understood [(2)]. Understanding these effects is essential for designing efficient ES-based extraction systems.

Previous work demonstrated that an L-proline:propylene glycol (1:4) ES containing 65 mol% water exhibits high extraction efficiency and selectivity toward salicylic acid from *Sargassum muticum* [(3)]. In this work, the molecular origin of this behaviour was investigated through solubility measurements and molecular dynamics simulations. The study was extended to other diol-based ES and their corresponding aqueous diol solutions. Additional hydroxybenzoic acids (HAs) were also evaluated to assess how the position and number of hydroxyl groups in the HA structure influence solubility behaviour. Interestingly, changes in solubility behaviour were observed for all diols when increasing the number of hydroxyl groups from two to three in the HA.

The results provide molecular-level insight into the role of water in structuring ES and modulating solute–solvent interactions, supporting the rational design of optimized ES-based extraction processes. The ES also showed strong tolerance to water addition, particularly regarding the preservation of HAs solvation shells.

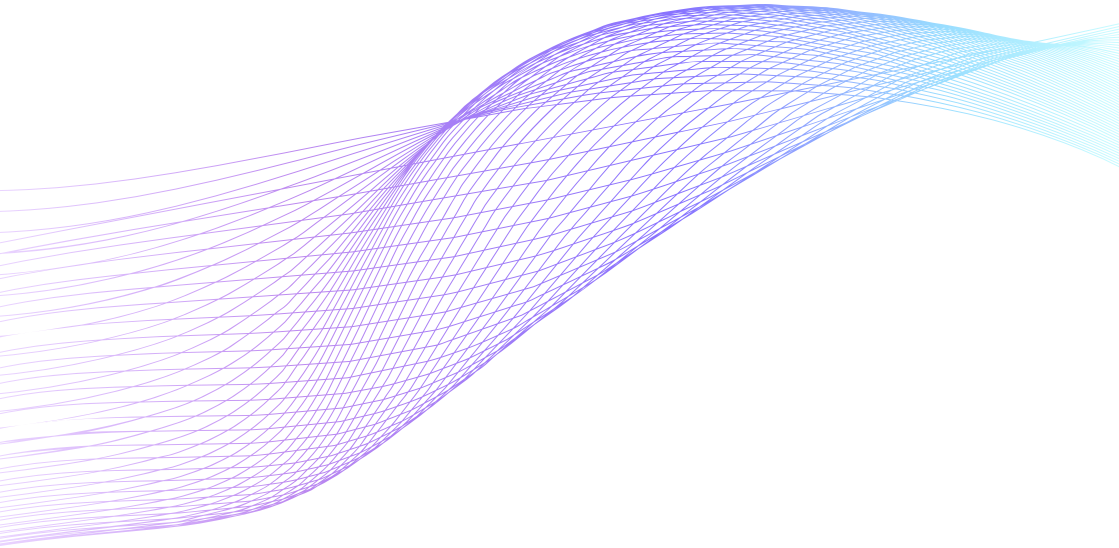
Acknowledgments

CQE (UIDB/00100/2020 and UIDP/00100/2020), IMS (LA/P/0056/2020), MARE (UIDP/04292/2020 and UIDB/04292/2020), ARNET (LA/P/0069/2020), N. Galamba (CEECIND/00821/2017 and 2023.07253.CEECIND/CP2831/CT0005) and Bárbara C. Jesus (Studentship 2023.00421.BD) are all funded by FCT.

References

(1) Soares, B., et al. *ACS Sustain. Chem. Eng*., 2019, **7**, 12485–12493; (2) Monteiro, H., et al. *ACS Sustain. Chem. Eng*., 2022, **10**, 3501–3512; (3) Jesus, B.C., et al. *RSC Sustainability,* 2023, **1**, 1245–1258.

POSTER COMMUNICATIONS



Effect of phenylation on the phase behavior of phenanthrene derivatives

C. S. T. Pinto[a]; L. M. N. B. F. Santos[a]; J. C. S. Costa[a]; C. F. R. A. C. Lima[a]
[a] *CIQUP, Institute of Molecular Sciences (*IMS*), Department of Chemistry and Biochemistry, Faculty of Science, University of Porto, Rua do Campo Alegre, P4169-007 Porto, Portugal.*
**e-mail: up202008144@up.pt*

This work focuses on the study of the phase behavior and cohesive energies of building blocks for organic semiconductors, underscoring the importance of molecular understanding of their crystal packing[1], namely: phenylphenathrene derivatives: 2-phenylphenanthrene, 9-phenylphenanthrene, and 2,7-diphenylphenanthrene. The compounds (Figure 1) were synthesized via the Suzuki-Miyaura cross-coupling reaction and their thermodynamic properties were characterized using Knudsen effusion combined with a quartz crystal microbalance (KNQ) alongside differential scanning calorimetry (DSC). DSC effectively resolved the solid-liquid phase behavior of all compounds and Knudsen effusion measurements provided precise vapor pressure data, enabling the determination of their sublimation thermodynamic properties.

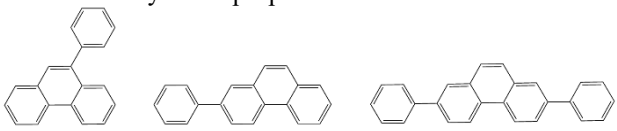


Figure 1: Structure of the phenanthrenes studied: (A) 9-Phenylphenanthrene; (B) 2-PhenylPhenanthrene; (C) 2,7-Diphenylphenanthrene

The results are compared with literature data reported for similar phenylanthracene derivatives. Two polymorphs were found for 9-phenylphenanthrene (A), while 2,7-diphenylphenanthrene (C) exhibited liquid-crystal transition before melting. It was found that the higher melting temperature and lower volatility of 2-phenylphenanthrene (B), compared to its 9-phenylphenanthrene (A) isomer, is entropically driven, associated with positional disorder within the crystal lattice.

Acknowledgments
The authors thank the Portuguese Foundation for Science and Technology (FCT) for financial support to CIQUP, Faculty of Science, University of Porto (Project UID/PRR/00081/2025, DOI https://doi.org/10.54499/UID/PRR/00081/2025), and IMS – Institute of Molecular Sciences (LA/P/0056/2020), Faculty of Science, University of Porto.

References
(1) Lima, C.F.R.A.C., et al. *J. Phys. Chem. B*, 2012. **116**, 3557–3570.

Functional group effects on leflunomide cocrystal formation: amide versus carboxylic acid coformers

N. A. S. Santos[a,*], J. A. Baptista[a], J. Canotilho[a,b], M. E. S. Eusébio[a], R. A. E. Castro[a,b], T. M. R. Maria[a]

[a] *University of Coimbra, CQC/IMS, Department of Chemistry, Coimbra, Portugal*
[b] *University of Coimbra, Faculty of Pharmacy, Coimbra, Portugal*
[*] *e-mail: nuno.alexandre.silva.santos@gmail.com*

Cocrystallisation is widely recognized as one of the most promising strategies for enhancing the aqueous solubility of poorly soluble active pharmaceutical ingredients (APIs). Cocrystals are multicomponent crystalline solids composed of two or more components in a defined stoichiometric ratio, with the individual components being solid at room temperature. Cocrystals of APIs exhibit different physical and chemical properties, while maintaining the intended therapeutic effect.[1] Leflunomide (LEF), Figure 1 (a), is a poorly water-soluble drug used in the treatment of rheumatoid arthritis. In this work, benzamide and benzoic acid, Figure 1 (b) and (c), respectively, were investigated as potential coformers. Cocrystallisation experiments were initially performed using a mechanochemical approach, which yielded physical mixtures for both systems. The resulting mixtures were recrystallized from ethyl acetate under ambient conditions, leading to the formation of small, plate-like crystals of a LEF-benzamide system. The resulting solids were characterized using X-ray powder diffraction (XRPD) and Fourier-transform infrared spectroscopy with attenuated total reflectance (FTIR-ATR). Single-crystal X-ray diffraction (SCXRD) enabled the crystal structure of the LEF-benzamide cocrystal to be determined. Structural analysis provided insight into the molecular arrangement and intermolecular interactions within the cocrystal, contributing to a better understanding of the solid-state behaviour of LEF and its ability to form multicomponent crystalline phases.

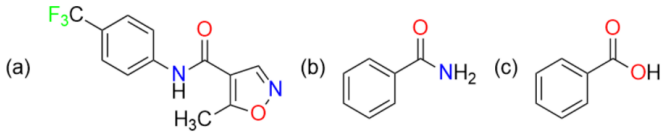


Figure 1: Molecular structures: (a) leflunomide; (b) benzamide; (c) benzoic acid

Acknowledgments
Coimbra Chemistry Center/Institute of Molecular Sciences (CQC/IMS) is supported by FCT, Foundation for Science and Technology (UIDB/00313/2020). Thanks are due to UCQFarma for the use of the PXRD facility. N.A.S.S. acknowledges FCT for financial support (Master grant UID/00313/2025). J.A.B. acknowledges FCT for financial support (PHD grant UI/BD/150859/2021).

References
(1) Karimi-Jafari, M.; Padrela, L., et al. *Cryst. Growth Des.* 2018, **18**, 6370–6387.

Phase behavior study of large phenyl acenes: phenylchrysene and phenyltriphenylene

A. P. Ferreira*, L. M. N. B. F. Santos, C. F. R. A. C. Lima
CIQUP, Institute of Molecular Sciences (IMS),
Department of Chemistry and Biochemistry, Faculty of Science, University of Porto,
Rua do Campo Alegre, 4169-007 Porto, Portugal
**e-mail: up202303726@up.pt*

This work investigates the phase behavior and thermodynamic properties of aromatic organic compounds containing a four-ring acene core, focusing on the influence of molecular structure on phase stability and phase transitions. A comparative analysis with structurally related compounds containing different acene cores and phenyl substituents was performed to identify systematic trends associated with the progressive extension of the π-conjugated framework.[1]

The compounds (Figure 1) were synthesized via Suzuki-Miyaura cross-coupling reactions, and their thermodynamic and phase behavior was investigated using Knudsen effusion combined with a quartz crystal microbalance (KNQ) and differential scanning calorimetry (DSC). All compounds were successfully synthesized and characterized, and their enthalpies and entropies of fusion and sublimation were determined, providing a thermodynamic description of the transitions between the condensed and gas phases. The occurrence of solid-solid phase transition was also investigated by DSC and optical microscopy.

The comparison of compounds containing different acene cores reveals consistent trends associated with the extension of the π-conjugated framework, which are reflected in their thermodynamic and structural properties. Overall, the results provide insight into the relationship between molecular architecture, phase equilibria, and π-electronic interactions in extended aromatic systems.

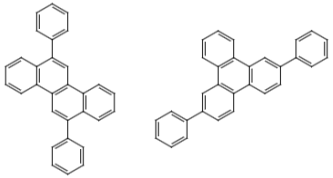


Figure 1: Structure of 6,12-diphenylchrysene (left) and 2,7-diphenyltriphenylene (right).

Acknowledgments
The authors thank to the Portuguese Foundation for Science and Technology (FCT) for financial support to CIQUP, Faculty of Science, University of Porto (Project UID/PRR/00081/2025, DOI https://doi.org/10.54499/UID/PRR/00081/2025), and IMS – Institute of Molecular Sciences (LA/P/0056/2020), Faculty of Science, University of Porto.

References
(1) Lima, C.F.R.A.C., et al. *J. Phys. Chem. B* 2012, **116**, 3557–3570.

Effect of a deep eutectic solvent and its constituents on tetrahydrofuran clathrate hydrates nucleation

A. P. Ferreira*, C. E. S. Bernardes, R. G. Simões, M. Tariq
Centro de Química Estrutural, Institute of Molecular Sciences, Departamento de Química e Bioquímica, Faculdade de Ciências, Universidade de Lisboa, 1749-016 Lisboa, Portugal
**e-mail: up202303726@up.pt*

The understanding of the formation of clathrate hydrates attracts a lot of attention due to their relevance in the energy (oil/gas) industry as well as in various environmental related applications.[1] The search for sustainable and green chemical additives that allow for the control over the formation of hydrates is also a current focus in this field. Therefore, in this work, the influence of choline chloride (ChCl), urea, and ChCl-urea (1:2) deep eutectic solvent (DES) on the formation and nucleation of tetrahydrofuran (THF) hydrates was investigated. THF clathrates form a structure similar to natural gas hydrates at atmospheric pressure, thereby it is frequently used as a model compound to screen the effect of various hydrate inhibitors/promoters.[2]

First, the ChCl-urea (1:2) DES was prepared and characterized using differential scanning calorimetry (DSC), infrared spectroscopy (IR), and thermogravimetric analysis (TGA). THF hydrate formation experiments were performed in absence/presence of additives using a constant cooling ramp methodology in an in-house built reactor. From these experiments, a large dataset of onset nucleation temperatures (T_{on}) of hydrates was obtained. The experimental data were further analysed to form the cumulative nucleation probability (F) distribution curves as a function of the degree of supercooling ($\Delta T = T_{eq} - T_{on}$, where T_{eq} is the equilibrium temperature). The nucleation rates (J) were deduced and the corresponding thermodynamic and kinetic parameters that govern the phase transition were also obtained. The results indicate that all the compounds investigated act as inhibitors of hydrate formation, with ChCl exhibiting the strongest inhibitory effect, followed by the DES and urea. Overall, this work opens up the possibility to study the effect of complex additives on clathrate hydrate nucleation in a systematic manner.

Acknowledgments
This work was supported by Fundação para a Ciência e Tecnologia (FCT) through projects UID/00100/2025 (https://doi.org/10.54499/UID/00100/2025), UID/PRR/00100/2025 (https://doi.org/10.54499/UID/PRR/00100/2025), and LA/P/0056/2020 (https://doi.org/10.54499/LA/P/0056/2020).

References
(1) Hassanpouryouzband, A., et al. *Chem. Soc. Rev.* 2020, **49**, 5225–5309.
(2) Liu, B., et al. *Energy & Fuels* 2022, **36**, 10642–10651.

Influence of solvent on the formation of distinct mefenamic acid-L-arginine solid forms

J. G. Santos[a,*], R. A. E. Castro[b], F. J. Caires[a]
[a] *São Paulo State University, Bauru, Brazil*
[b] *University of Coimbra, Coimbra, Portugal*
[*] *e-mail: juliana.guedes@unesp.br*

Mefenamic acid (MFA) is an active pharmaceutical ingredient (API) belonging to the class of non-steroidal anti-inflammatory drugs (NSAIDs), recognized for its analgesic, anti-inflammatory, and antipyretic actions.[1,2] MFA is classified by the Biopharmaceutics Classification System as class II, which means it exhibits high permeability and low solubility in aqueous media, limiting its bioavailability and potentially causing side effects.[1,2] The development of multicomponent solid forms emerges as a strategy to modulate the physicochemical properties of drugs such as MFA through intermolecular interactions between the API and a molecule termed a coformer, where the solvent may influence the establishment of these interactions and the resulting crystal structure[1,3]. In this context, the present study investigated the synthesis and characterization of multicomponent solid forms of MFA with L-arginine (ARG), evaluating the role of the solvent in the resulting solid. The systems were synthesized via liquid-assisted grinding of the precursors in a 1:1 molar ratio in a vibratory ball mill at 30 Hz for 30 min, employing water, ethanol, and an ethanol:water binary mixture. The precursors and resulting solid forms were characterized by Thermogravimetry and Differential Thermal Analysis (TG-DTA), Differential Scanning Calorimetry (DSC), Powder X-ray Diffraction (PXRD), and Fourier-Transform Infrared Spectroscopy (FTIR). The PXRD patterns confirmed the formation of three distinct crystalline structures, demonstrating that each solvent leads to a new supramolecular arrangement. The FTIR spectra indicated the appearance, disappearance, and shifts of characteristic bands, indicating specific intermolecular interactions in each system. Thermal analysis showed that the thermal behavior of the systems differs from the precursors, while displaying some similarities among themselves. These results prove that the choice of solvent is a critical parameter governing crystal structure formation and for the modulation of the properties of MFA-ARG systems.

Acknowledgments
This research was financially supported by the Sao Paulo Research Foundation (FAPESP) [grant numbers: 2026/08421-5 and 2025/01945–6].

References
(1) Zhang, X.R., et al. *J. Mol. Struct* 2025, **1340**, 142605.
(2) Kumar, V., et al. *Front. Chem* 2022, **10**, 729608.
(3) Vioglio, P.C.; Chierotti, M.R.; Gobetto, R. *Drug Deliv. Rev* 2017, **117**, 86–110.

Structural and thermal characterization of pharmaceutical cocrystals and co-amorphous systems

S. P. Gonçalves[a,*], P. S. P. Silva[a], M. R. Silva[a], M. T. S. Rosado[b], T. M. R. Maria[b], M. E. S. Eusébio[b]

[a] *CFisUC, Department of Physics, University of Coimbra, Coimbra, Portugal*
[b] *Coimbra Chemistry Center/Institute of Molecular Sciences, Department of Chemistry, University of Coimbra, Coimbra, Portugal*
[*] *e-mail: sofiapaulinogoncalves@gmail.com*

The solid-state form of an active pharmaceutical ingredient (API) strongly influences its solubility, stability and bioavailability.[1] In this work, pharmaceutical cocrystals and co-amorphous systems were investigated through a combination of single-crystal X-ray diffraction (SCXRD), powder X-ray diffraction (PXRD) and thermogravimetric analysis (TGA), with the aim of correlating crystal structure, intermolecular interactions and thermal behaviour. SCXRD enabled the determination of two new crystal structures: the 2:1 theophylline:2,4-diaminopyrimidine cocrystal and the 1:1 lamotrigine:ethosuximide cocrystal (Figure 1). PXRD confirmed the formation of new phases in the 1:1 ibuprofen:nicotinamide and 2:1 naproxen:nicotinamide systems. Rietveld refinement further confirmed the formation of the naproxen:nicotinamide cocrystal and identified the polymorphic composition of pyrimethamine-based systems. Long-term PXRD monitoring of the 1:1 domperidone:hypoxanthine system revealed the gradual crystallization of an initially co-amorphous material. TGA complemented the structural analysis by allowing the thermal transitions and melting enthalpies of selected cocrystals to be determined.

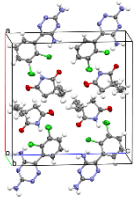


Figure 1: Unit cell of the 1:1 lamotrigine:ethosuximide cocrystal

Acknowledgments
Access to TAIL-UC facility funded under QREN-Mais Centro Project ICT/2009/02/012/1890 is gratefully acknowledged.

References
(1) Baptista, J.A.; Castro, R.A.E.; Rosado, M.T.S.; Maria, T.M.R.; Silva, M.R.; Canotilho, J.; Eusébio, M.E.S. *Cryst. Growth Des.* 2021, **21**, 3699–3713.

THEDES Phase transition dynamics for enhanced tuberculosis treatment

T. Alves[a,*], D. Alves[b], A. Granja[a], M. Borges[b], C. Nunes[a], S. Reis[a], M. Sarraguça[a]

[a] *LAQV-REQUIMTE, Faculty of Pharmacy of the University of Porto, Portugal*
[b] *UCIBIO, Faculty of Pharmacy of the University of Porto, Portugal*
[*] *e-mail: up201704456@up.pt*

Tuberculosis (TB), caused by Mycobacterium tuberculosis (Mtb), remains a major global health challenge, with 10.7 million cases annually.[1] Its persistence is partly associated with Mtb's ability to survive as dormant bacilli within granulomas, where first-line drugs such as isoniazid, which primarily target active metabolic processes, have limited effectiveness, contributing to the need for prolonged treatment regimens.[2]

Therapeutic Deep Eutectic Solvents (THEDES), in which a drug is incorporated as a component of a Deep Eutectic Solvent (DES), represent a promising strategy to improve drug delivery. DESs are non-ideal eutectic mixtures characterized by a significant melting-point depression, often remaining liquid at room temperature.[3] By leveraging their unique physicochemical properties, specifically their tunable phase transitions, THEDES can be engineered to dramatically upgrade the bioavailability and cellular permeability of anti-TB drugs.[3] These innovative systems could facilitate deeper drug penetration into granulomas, ensuring active pharmaceutical ingredients reach and neutralize even dormant Mtb populations.

This study presents a novel therapeutic platform by incorporating isoniazid and glucose into the THEDES formulation. The system exploits unique phase transition properties to significantly enhance drug solubility and bioavailability. Simultaneously, glucose can serve as an awakening agent to reactivate dormant bacilli inside hypoxic granulomas, rendering them vulnerable to therapy. The developed formulation was characterized regarding physicochemical properties, stability, and *in vitro* performance.

Acknowledgments

This work received financial support from the project "Eutectic Solutions for Controlled and Advanced Pulmonary Enhancement in Tuberculosis", with reference COMPETE2030-FEDER-00662700, operation 15566, supported by FEDER (COMPETE 2030) and national funds by FCT / MCTES.

References

(1) World Health Organization. Tuberculosis. 2025. (accessed 12/12/2025).
(2) Dartois, V. A.; Rubin, E.J. *Nature Reviews Microbiology* 2022, **20**, 685–701.
(3) Li, K.; Yan, B.; Cao, Z.; Lu, R.; Wu, G.; Hai, Y. *Pharmaceutics* 2026, **18**, 360.

Solid-state characterisation of aromatic azides: from cryogenic crystallisation to periodic DFT modelling

R. R. Neves[a,*], J. A. Paixão[b], C. M. Nunes[a], M. T. S. Rosado[a]
[a] *University of Coimbra, CQC- IMS, Department of Chemistry, Coimbra, Portugal*
[b] *University of Coimbra, CFisUC, Department of Physics, Coimbra, Portugal*
[*] *e-mail: rafael.neves@qui.uc.pt*

Aromatic azides constitute an important class of highly reactive compounds with applications in synthetic chemistry, materials science, energetic materials and photochemical processes. Their structural versatility and sensitivity to external stimuli make the study of their solid-state properties particularly relevant. In this work, several aromatic azides were investigated through a combined experimental and computational approach aimed at characterising their crystalline forms and vibrational behaviour. Crystalline phases were obtained either by annealing amorphous solids deposited under cryogenic conditions or by solvent evaporation. The resulting materials were characterised by in situ infrared cryospectroscopy, differential scanning calorimetry (DSC) and single-crystal X-ray diffraction (SCXRD). To support the experimental observations, density functional theory (DFT) calculations were performed on isolated molecules and periodic crystal structures, enabling the interpretation of vibrational spectra and the estimation of lattice-related effects. The comparison between matrix-isolated species, crystalline phases and theoretical models revealed clear spectroscopic signatures associated with crystallisation and intermolecular interactions in the solid state. Periodic DFT calculations showed good agreement with the experimental infrared spectra, demonstrating their value for the assignment of vibrational modes and the study of crystal packing effects. These results contribute to a deeper understanding of the structure-property relationships of aromatic azides and provide a framework for future investigations of their solid-state behaviour and reactivity.

Acknowledgments
We acknowledge funding from the Coimbra Chemistry Centre – Institute of Molecular Sciences (CQC-IMS) which is supported by the Fundação para a Ciência e a Tecnologia (FCT), Portuguese Agency for Scientific Research. CQC is funded by FCT through projects UID/PRR/00313/2025, UID/PRR2/00313/2025 and UID/00313/2025, and IMS through special complementary funds provided by FCT (project LA/P/0056/2020). Also the Project 2023.11222.PEX (https:// doi. org/10. 54499/ 2023.11222. PEX) funded by the Fundação para a Ciência e a Tecnologia (FCT). RRN acknowledges FCT for a PhD grant (UID/00313/2025).

Experimental and numerical study of ternary systems MSO_4-$M'SO_4$-H_2O (M, M' = Li_2, Ni, Co)

N. Patry[a], A. Lassin[b,c], L. Andre[b,c], Y. Cartigny[a], N. Couvrat[a*]
[a] *Univ Rouen Normandie, Normandie Univ, SMS, UR 3233, France*
[b] *BRGM – French Geological Survey, F-45060 Orléans, France,*
[c] *ISTO, UMR 7327, Univ Orléans, CNRS, BRGM, OSUC, F-45071 Orléans, France*
**e-mail: nicolas.couvrat@univ-rouen.fr*

Cobalt, nickel, and lithium sulfate salts are compounds used in the manufacture of lithium-ion batteries (LiBs). Recycling processes for these metals (Li, Co, Ni) are already well-established, involving their dissolution in sulfuric acid. However, the chemical behavior of such electrolyte solutions and the associated solid-liquid equilibria remain poorly described.

This study aims to improve the thermodynamic description of ternary systems MSO_4–$M'SO_4$–H_2O (M, M' = Li_2, Ni, Co) by combining experimental and modeling approaches for temperatures ranging from 10 to 50°C. Initially, the binary systems $NiSO_4$–H_2O, $CoSO_4$–H_2O, and Li_2SO_4–H_2O were studied over this same temperature range. Several isothermal sections of the phase diagram were then determined for the ternary systems based on solid-liquid equilibria obtained using a device designed in the laboratory, called D.I.T.A. (Discontinuous Isoperibolic Thermal Analysis).[1]

In terms of modeling, given the high salinities of the solutions, a Pitzer-type approach was chosen to accurately describe the activity coefficients of the aqueous species. Based on the existing Pitzer-specific interaction parameters for the three binary systems, the experimental data acquired during this study[2] were used to optimize new ternary interaction parameters.

References

(1) Marchand, P.; Lefebvre, L.; Courvoisier, L.; Perez, G.; Counioux, J.-J.; Coquerel, G. *J. Phys. IV* 2001, **11**, Pr10-115–Pr10-122.
(2) Patry, N.; Hébert, N.; Peulon-Agasse, V.; Lassin, A.; André, L.; Couvrat, N.; Cartigny, Y. *J. Chem. Eng. Data* 2025, **70**, 1490–1497.
(3) Patry, N.; Lassin, A.; André, L., et al. *J. Chem. Therm*. 2026, 107650.
(4) Lach, A.; Boulahya, F.; André, L.; Lassin, A.; Azaroual, M.; Serin, J.P.; Cézac, P. *Comput. & Geosci*. 2016, **92**, 58–69.

Structure, stability and solubility of a new monomethyl fumarate:nicotinamide bicomponent crystal

M. F. M. Piedade*, R. L. Mané, R. G. Simões, M. E. Minas da Piedade
Centro de Química Estrutural, Institute of Molecular Sciences, Faculdade de Ciências, Universidade de Lisboa, Campo Grande, 1749-016 Lisboa, Portugal
**e-mail: fc62064@alunos.ciencias.ulisboa.pt*

Monomethyl fumarate (MMF) is a clinically relevant bioactive compound used in the treatment of multiple sclerosis and increasingly explored for a broad range of therapeutic applications whose crystal structure and thermodynamic stability were recently investigated.[1] Here, we report on the successful mechanochemical preparation of a new 1:1 co-crystal of MMF with nicotinamide (NIC). The obtained MMF:NIC material was comprehensively characterized in terms of structure, thermal behavior, stability, and solubility performance. Single-crystal X-ray diffraction confirmed the formation of the 1:1 co-crystal and provided detailed insight into its supramolecular arrangement (Figure 1). Thermal analysis and calorimetric characterization supported the stability of the co-crystal against dissociation into its individual co-formers. Solubility studies demonstrated a marked enhancement in MMF solubility upon co-crystallization with NIC.

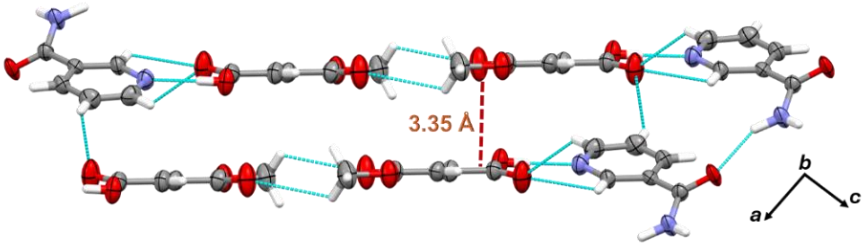


Figure 1: 3D crystal packing of MEF:NIC showing key hydrogen bond interactions

Acknowledgments
This work was supported by Fundação para a Ciência e a Tecnologia (FCT) through projects LA/P/0056/2020 (DOI https://doi.org/10.54499/LA/P/0056/2020), UID/00100/2025 (https://doi.org/10.54499/UID/00100/2025), UID/PRR/100/2025 (https://doi.org/10.54499/UID/PRR/00100/2025),

References
(1). Évora, A.O.L; Valente-Matias, D.F.; Bernardes, C.E.S.; Lousada, C.M.; Piedade, M.F.M.; Lusi, M.; Diogo, H.P.; Minas da Piedade, M.E. *Cryst. Growth Des.* 2024, **24**, 9465–9481.

Monoethyl fumarate in water: from solubility curve to liquid-liquid phase separation

D. N. G. Palma*, R. G. Simões, C. E. S. Bernardes, M. E. Minas da Piedade

Centro de Química Estrutural, Institute of Molecular Sciences, Faculdade de Ciências, Universidade de Lisboa, Campo Grande, 1749-016 Lisboa, Portugal

**e-mail: fc62064@alunos.ciencias.ulisboa.pt*

In the pharmaceutical sector, aqueous solubility is a fundamental property that often dictates a drug's therapeutic success. Fumaric acid and alkyl fumarates are a family of structurally related compounds with a remarkable success in the treatment of psoriasis and multiple sclerosis, and promising therapeutic potential for various other diseases. As part of our studies on this family,[1, 2] here we present the determination of the monoethyl fumarate (MEF)-water *T*-*x* phase diagram. The results suggest that it is of the monotetic type illustrated in Figure 1: up to $x \sim 0.02$ ($T > 297$ K) the solid-liquid equilibrium curve follows an exponential relationship. Above that concentration, however, liquid-liquid phase separation is observed, followed by a considerable solubility increase. This perturbation occurs close to ambient temperature and can, therefore, complicate the control of MEF aqueous solubility if the compound is to be formulated as a drug.

The experimental work was complemented by molecular dynamics simulations at various relevant concentrations to investigate the molecular-scale arrangements involved in this phenomenon.

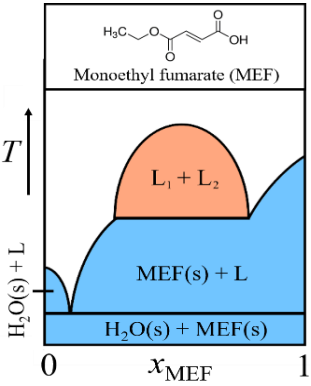


Figure 1: MEF structure and expected *T*-*x* phase diagram

Acknowledgments

This work was supported by Fundação para a Ciência e a Tecnologia (FCT) through projects LA/P/0056/2020 (DOI https://doi.org/10.54499/LA/P/0056/2020), UID/00100/2025 (https://doi.org/10.54499/UID/00100/2025), UID/PRR/100/2025 (https://doi.org/10.54499/UID/PRR/00100/2025), UID/PRR2/00100/2025 (https://doi.org/10.54499/UID/PRR2/00100/2025), and 2023.15441.TENURE.004/CP00003/CT00002.

References

(1) Évora, A.O.L.,et al. *Cryst. Growth Des.*, 2019, **19**, 5054–5064.

(2) Évora**,** A.O.L.,et al. *Cryst. Growth Des.* 2024, **24**, 9465–9481.

Deep eutectic solvents as tunable media for enhancing the solubility of quercetin

R. Costa[a], R. Maduro[a], S. Reis[a], M. Passos[a], M. Sarraguça[a,*]
[a] *LAQV-REQUIMTE, Faculty of Pharmacy of the University of Porto, Portugal*
[*]*e-mail: mafalda.cruz@ff.up.pt*

Poor aqueous solubility limits the formulation and biomedical application of many bioactive compounds. Quercetin is a naturally occurring flavonoid with antioxidant, anti-inflammatory, antimicrobial, and immunomodulatory properties,[1] with potential as a therapeutic adjuvant in several diseases, including tuberculosis.[2] However, its application is strongly limited by its poor aqueous solubility and low bioavailability. Deep eutectic solvents (DES) have emerged as alternative media for improving the solubility of poorly water-soluble compounds. DES are eutectic mixtures that exhibit negative deviations from ideal thermodynamic behavior due to strong intermolecular interactions between their components. These interactions, particularly hydrogen bonding, induce a pronounced melting-point depression, allowing the mixtures to remain liquid at room temperature.[3] Their properties can be tailored by varying their composition and molar ratio, providing versatile solvation environments. In this work, hydrated betaine:glucose systems and a urea:lactic acid DES were evaluated for the solubilization of quercetin. Quercetin was quantified by UV-Vis spectrophotometry after equilibration in the different media. All investigated DES substantially enhanced quercetin solubility compared with aqueous media, with increases approaching one order of magnitude. These results demonstrate the potential of DES as a tunable solvent platform for formulating poorly water-soluble bioactive compounds.

Acknowledgments
This work received financial support from the project "Eutectic Solutions for Controlled and Advanced Pulmonary Enhancement in Tuberculosis", with reference COMPETE2030-FEDER-00662700, operation 15566, supported by FEDER (COMPETE 2030) and national funds by FCT / MCTES.
M.S and M.P. thank the Individual Call to Scientific Employment Stimulus (DOI 10.54499/2022.01388.CEECIND/CP1724/CT0003 and DOI 10.54499/2021.00921.CEECIND/CP1662/CT0005). The authors thank the support from the PT national funds (FCT/MECI), project UID/50006/2025 DOI 10.54499/UID/50006/2025-Laboratório Associado para a Química Verde - Tecnologias e Processos Limpos.

References
(1) Wang, W.; Sun, C.; Mao, L.; Ma, P.; Liu, F.; Yang, J.; Gao, Y. *Trends Food Sci. Technol.* 2016, **56**, 21–38.
(2) Sasikumar, K.; Ghosh, A.R.; Dusthackeer, A. 3 *Biotech* 2018, **8**, 10.
(3) Smith, E. L.; Abbott, A.P.; Ryder, K.S. *Chem. Rev*. 2014**, 114**, 11060–11082.

Molecular dynamics of carbonic anhydrase II in choline:urea-based deep eutectic solvents

D. J. M. Agostinho[a,*], M. M. Pereira[a], M. E. Ghica[a]
[a] *University of Coimbra, CERES, Department of Chemical Engineering, Pólo II, Rua Sílvio Lima, 3030-790 Coimbra, Portugal*
[*] *e-mail: daniel.marques.agostinho@gmail.com*

Carbonic anhydrase II (CA II) is a zinc-dependent metalloenzyme whose catalytic Zn^{2+} centre and surrounding residues define a solvent-accessible active site.[1] Deep eutectic solvents (DES) are increasingly investigated as tunable media for biomolecular applications and have shown potential as reaction environments for carbonic anhydrase.[2] Yet the molecular basis of protein-DES interactions remains incompletely understood. Here, 250 ns molecular dynamics simulations were used to examine the response of bovine CA II to urea, choline chloride (ChCl), choline acetate (ChOAc), choline dihydrogen citrate (ChDHC), and the corresponding 1:2 choline:urea-based DES formulations ChCl:Urea, ChOAc:Urea, and ChDHC:Urea. Protein behaviour was assessed through global and residue-level structural descriptors, hydrogen-bonding patterns, mobility of the Zn^{2+}-coordination environment, and the local composition of the protein-solvent interface.

The simulations demonstrate that choline:urea DES preserve the global structural stability of CA II while modulating its local dynamics in a formulation- and protonation-dependent manner. Although the protein maintained its overall fold, compactness, and hydrogen-bond network, DES reduced global conformational mobility and altered local flexibility, including near the catalytic metal-coordination site. Notably, no clear evidence of persistent binding or active-site blockage was observed. These findings indicate that DES can influence enzyme dynamics without compromising the protein scaffold, providing a molecular basis for understanding and optimizing alternative solvent systems for enzyme applications.

Acknowledgements
Work developed under the project 3DBIOGEL4HEALTH – "Exploring the 3D Bioprinting for Design of Novel Biodegradable Hydrogels as Lutein Carriers," funded by national funds through the Foundation for Science and Technology (FCT) – Ref. No. 2023.12614.PEX.

References
(1) Saito, R.; Sato, T.; Ikai, A.; Tanaka, N. *Acta Crystallogr. D Biol. Crystallogr.* 2004, **60**, 792-795.
(2) Zhou, Y.; Wu, Y.-J.; Wang, L.; Han, J.; Wu, J.-C.; Li, C.-M.; Wang, Y. *Int. J. Biol. Macromol.* 2021, **190**, 206-213.

Accelerating OpenCOSMO-RS with graph convolutional networks

R A. F. Serrano[a], S. Müller[b], I. Smirnova[b], J. A. P. Coutinho[a], D. O. Abranches[a,*]

[a] *University of Aveiro, Campus Universitário de Santiago, 3810-193, Aveiro, Portugal*
[b] *Institute of Thermal Separation Processes, Hamburg University of Technology, Eißendorfer Straße 38, Hamburg, Germany*
[*] *e-mail: jdinis@ua.pt*

Sigma profiles are the foundational input to COSMO-RS, but their generation requires expensive quantum-chemical calculations. We developed a machine learning model for openCOSMO-RS,[1] an open-source implementation of COSMO-RS, that replaces this quantum-chemical step using graph convolutional networks (GCNs), allowing to predict the descriptors required by openCOSMO-RS from SMILES-derived molecular graphs. A database of 12930 neutral and ionic compounds spanning 36 elements was generated with ORCA 6.0.

Surface charge densities averaged over radii of 0.5 and 1.0 Å were encoded as a 78 × 78 sigma matrix and compressed to 1595 dimensions. Four distinct Bayesian-optimized GCN models, with architectures based on previous work,[2] predicted this vector and COSMO cavity volume using atomic-number or MMFF atom-type as node-level featurization.

MMFF-based models achieved test-set R^2 values of 0.93 for the sigma matrix and 1.00 for cavity volume. Reconstructed profiles reproduced the main polar and apolar regions of glycerol and choline, typical deep eutectic solvent precursors.

Reparameterization of openCOSMO-RS using the GCN-derived descriptors is underway and will be completed in this study. This final stage will establish an open-source workflow for high-throughput thermodynamic screening.

Acknowledgments

The work was developed within the scope of the project CICECO-Aveiro Institute of Materials, UID/50011/2025 (10.54499/UID/50011/2025) and LA/P/0006/2020 (10.54499/LA/P/0006/2020) and UID/PRR/50011/2025 (10.54499/UID/PRR/50011/2025), financed by national funds through the FCT/MCTES (PIDDAC).

References

(1) Müller, S.; Nevolianis, T.; Garcia-Ratés, M.; Riplinger, C.; Leonhard, K.; Smirnova, I. *Fluid Ph. Equilib.* 2025, **589**, 114250.

(2) Abranches, D. O.; Maginn, E. J.; Colón, Y. J. *J. Chem. Theory Comput.* 2023, **19**, 9318–9328.

Phase equilibrium properties of binary systems (furfural + alcohols) at several temperatures

N. Chiali[a,*], A. Negadi[a], J. Jose[b], I. Mokbel[b], L. Negadi[a,c]

[a] *LATA2M, Laboratoire de Thermodynamique Appliquée et Modélisation Moléculaire, University of Tlemcen, Post Office Box 119, Tlemcen 13000, Algeria*

[b] *Laboratoire Multimatériaux et Interfaces, UMR 5615, Université de Lyon, Université Claude Bernard-Lyon1, 69622 Villeurbanne, France*

[c] *Thermodynamics Research Unit, School of Engineering, University of KwaZulu-Natal, Howard College Campus, King George V Avenue, 4041 Durban, South Africa*

[*] *e-mail: nouriabdz@yahoo.fr, Nouria.babaahmed@univ-tlemcen.dz*

The vapor pressures of the binary mixtures (furfural + ethanol) and (furfural + butan-2-ol) along with the pure component ethanol were measured using the static apparatus for VLE measurements (static device) between temperatures of 283 and 363 K. The generated results from this work were correlated using semi-empirical correlations as described by the Antoine equation. The excess Gibbs function was computed at assorted constant temperatures and applied to fit a fourth-order Redlich−Kister equation utilizing the Barker's technique, as these two systems in study exhibited positive deviations in GE at all temperatures studied over the whole composition range. The Modified UNIFAC (Do) model, UNIQUAC model, and the NRTL model together with the Peng-Robinson-Sheng-Lu equation of state (PRSL EoS) were also employed, and excellent results were observed in the modeling of the total pressure. The Redlich−Kister equation was applied successfully for modeling the thermodynamic excess properties.

Acknowledgments

The authors (N.L.) and (N.A.) acknowledge funding from DGRSDT (Algeria) and MESRS (Algeria).

References

(1) Chiali-Baba Ahmed, N.; Mokbel, I.; Negadi, A., Hernandez, A.; Jose, J.; Mo-hal, T.; Bahadur; I.; Mohammad, F.; Negadi, L. *J. Chem. Eng. Data* 2023, **68**, 2888–2897.

(2) Bendiaf, L.; Negadi, A.; Mokbel, I.; Negadi, L. *Fuel* 2014, **122**, 247−253.

Modeling excess molar enthalpies of dimethyl carbonate with eight hydrocarbons

N. Chiali[a,*], A. Negadi[a], J. Jose[b], L. Negadi[a,c]

[a] *LATA2M, Laboratoire de Thermodynamique Appliquée et Modélisation Moléculaire, University of Tlemcen, Post Office Box 119, Tlemcen 13000, Algeria*

[b] *Laboratoire Multimatériaux et Interfaces, UMR 5615, Université de Lyon, Université Claude Bernard-Lyon1, 69622 Villeurbanne, France*

[c] *Thermodynamics Research Unit, School of Engineering, University of KwaZulu-Natal, Howard College Campus, King George V Avenue, 4041 Durban, South Africa*

[*] *email: nouriabdz@yahoo.fr, Nouria.babaahmed@univ-tlemcen.dz*

Experimental excess molar enthalpies (H^E_m) for binary mixtures of{dimethylcarbonate(DMC) with benzene or isopropylbenzene or n-heptane or cyclohexane or hex-1-yne or hex-2-yne or hex-3-yne}over the whole composition range, are reported in this work.

Furthermore, the measured data were fitted to the Redlich−Kister equation. Additionally, the NRTL, UNIQUAC, UNIFAC models (semipreditcive)and PC-SAFT(predictive method) were used to correlate the excess molar enthalpy of the investigated systems.The results showed good agreement with the experimental enthalpy data. PC-SAFT yielded good qualitative results for the mixtures studied, and good quantitative results for some of them.

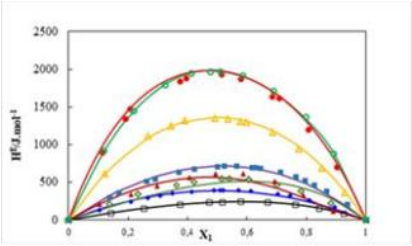


Figure 1. Comparison between experimental excess molar enthalpy, H^E_m and calculated using NRTL (—) model for the binary mixture, as a function of mole fraction of (dimethylcarbonate + hydrocarbon). The curves for binary mixture are represented by :benzene (◆),isopropylbenzene (■), n-heptane (o).Cyclohexane (●), Hex-1-ene (Δ),hex-1-yne (□), hex-2-yne (◊) and Hex-3-yne (▲)

Acknowledgements

The authors (N.L.) and (N.A.) acknowledge funding from DGRSDT (Algeria) and MESRS (Algeria).

References

(1) Negadi, L.; Blondel, A.; Mokbel, I.; Ait-Kaci, A.; Jose, J. *Int. DATA Ser., Sel. Data Mixtures, Ser. A* 1993, **21**, 164–194.

Thermophysical characterization of DMSO-based binary mixtures

F. Ouaar[a], N. Chiali[a,*], A. Negadi[a] , L. Negadi[a,b]
[a] *LATA2M, Laboratoire de Thermodynamique Appliquée et Modélisation Moléculaire, University of Tlemcen, Post Office Box 119, Tlemcen 13000, Algeria*
[b] *Thermodynamics Research Unit, School of Engineering, University of KwaZulu-Natal, Howard College Campus, King George V Avenue, 4041 Durban, South Africa*
[*] *e-mail: nouriabdz@yahoo.fr, Nouria.babaahmed@univ-tlemcen.dz*

Amines are an important class of compounds used in different fields of industry, they represent a particularly interesting family of molecules for the purpose of testing group-contribution models, and analyze the intramolecular effects, especially the proximity effect.
The present work is part of a research program on thermodynamic and thermophysical properties of binary mixtures containing amines or alcanolamines. In this paper, we report the experimental densities, speeds of sound, and refractive indices for four binary mixtures: DMSO + methylethanolamine (MEA), or + benzylamine, or + 3-dimethylaminol-1-propanol, or + 2-[2-(dimethylamino-ethoxy-tehanol)] measured over the entire composition range and in the temperatures range (293.15 to 323.15) K at 10 K intervals. From these experimental data, excess molar volume, isentropic compressibility, excess isentropic compressibility, refractive index deviation, excess refractive index, molar refraction, and molar refraction deviation have been calculated over the entire composition range and at each temperature. Excess molar volume, excess isentropic compressibility, excess speed of sound, excess refractive index, and molar refraction deviation data have been correlated using the Redlich−Kister equation. The thermodynamic properties have been discussed in terms of the nature of molecular interactions between the components of the mixture.

References:

(1) Kohl, A.L.; Nielsen, R. *Gas Purification*, fifth ed., Gulf Publishing Co., Houston, 1997.
(2) Camper, D.; Bara, J.E.; Gin, D.L.; Noble, R.D. *Ind. Eng. Chem. Res*. 2008, **47**, 8496–8498.
(3) Valtz, A.; Coquelet, C.; Richon, D. *Thermochim. Acta* 2005, **428**, 185–191.

Experimental excess molar enthalpies and thermodynamic analysis of binary mixtures of 1-butanol with glycol ethers

K. Samadi[a,b*], M. Lifi[c], H. Lifi[d], F. Aguilar[b], F. E. M'hamdi Alaoui[a]
[a] *Energy Laboratory, Faculty of Sciences, University of Abdelmalek Essaadi, Tetouan, Morocco*
[b] *Departamento de Ingeniería Electromecánica, Escuela Politécnica Superior, Universidad de Burgos, Spain, Burgos*
[c] *Department of Mathematics and Computing, Faculty of Science, University of Burgos, Spain, Burgos*
[d] *MISCOM Laboratory, National School of Applied Sciences, Cadi Ayyad University, B.P. 46000, Safi, Morocco*
[*] *e-mail: ksx1021@alu.ubu.es*

The excess molar enthalpy of three binary mixtures, namely 2-phenoxyethanol (2-PhE) + 1-butanol (1-BuOH), 2-ethoxyethanol (2-EE) + 1-butanol, and 2-(2-ethoxyethoxy)ethanol (22EEE) + 1-butanol, was experimentally determined over the entire composition range at atmospheric pressure using a quasi-isothermal flow calorimeter. Measurements were carried out at 298.15 K and 313.15 K, ensuring reliable and reproducible thermodynamic data. The results show positive H_m^E values for all systems, indicating endothermic mixing and significant deviations from ideality. These effects are mainly attributed to the disruption of self-associated hydrogen-bonding structures in the pure components and the formation of weaker hetero-interactions between unlike molecules, as well as the influence of molecular size and polarity.

The experimental data were correlated using the Redlich-Kister equation and modeled with NRTL and UNIQUAC approaches, while the predictive capability of the modified UNIFAC (Dortmund) model was also evaluated. Among the applied models, the Redlich-Kister equation provided the best agreement with experimental data, followed by NRTL and UNIQUAC, whereas UNIFAC showed limited predictive performance due to its inability to accurately represent specific interactions[1,2]. Overall, the results contribute to a better understanding of molecular interactions in glycol ether-alcohol systems and provide valuable thermodynamic data for process design and modeling.

Acknowledgments
The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References
(1) Prausnitz, J.M. 3rd ed.; Prentice Hall PTR: Upper Saddle River, N.J, 1999.
(2) Poling, B.E.; Prausnitz, J.M.; O'Connell, J.P. Fifth edition; McGraw-Hill Education: New York, N.Y, 2020.

Measurements and modeling of the physico-chemical properties of 1,2-dimethoxyethane and its binary mixtures with various alcohols

N. L. Benkalfat-Seladji[a], N. C. Baba-Ahmed[a], A. Belabbaci[a,*]
A. Negadi[a], L. Negadi[a,b]
[a] *LATA2M, Laboratoire de Thermodynamique Appliquée et Modélisation Moléculaire, University of Tlemcen,PostOfficeBox 119, Tlemcen 13000,Algeria*
[b] *Thermodynamics Research Unit, School of Engineering, University of KwaZulu-Natal, Howard College Campus, King George V Avenue, 4041 Durban, South Africa.*
[*] *e-mail: aouicha_belabbaci@yahoo.fr*

Glycol ethers are compounds widely used in industrial and medical fields. In this work, we determined the thermophysical properties of 1,2-dimethoxyethane as well as its binary mixtures with several alcohols (methanol, propan-1-ol, propan-2-ol, and butan-2-ol). We measured the density (ρ), speed of sound (u), and refractive index (n_D) at atmospheric pressure over a temperature range from 293.15 K to 323.15 K across the entire composition range at a pressure of 0.1 MPa.

This will allow us to explore the molecular interactions between the different components. Excess properties, such as excess molar volumes (V^E) and various derived properties, including isentropic compressibility, deviation in isentropic compressibility (ΔK_S), and deviation in refractive index (Δn_D), were calculated using the obtained experimental values. All excess and derived properties were correlated using the Redlich–Kister polynomial.

To model the different measured properties of pure components and their mixtures, we applied various equations of state, such as PSRK, VTPR, and CPA.

Thermodynamic, ultrasonic, and transport study of binary mixtures containing 1-hexene and alcohols at (293.15 - 303.15) K

A. Belabbaci[a,*], K. N. Abdellaoui[a], A. Ayad[a], A. Negadi[a], L. Negadi[a,b]
[a] *LATA2M, Laboratoire de Thermodynamique Appliquée et Modélisation Moléculaire, University of Tlemcen,PostOfficeBox 119, Tlemcen 13000,Algeria*
[b] *Thermodynamics Research Unit, School of Engineering, University of KwaZulu-Natal, Howard College Campus, King George V Avenue, 4041 Durban, South Africa.*
**aouicha.belabbaci@univ-tlemcen.dz*

Alcohol fuels can be an alternative source of environmentally friendly fuels to reduce exhaust emissions by using renewable energy in different countries of the world. Hydrocarbons/alcohols mixtures constitute crucial products in industry and remarkable systems from the thermodynamic point of view. Within this framework, light alcohols are frequently used as blending agent in the formulation new gasoline, taking into account environmental constraints, to both partly replace for hydrocarbon car fuels and augment their octane number while enhancing vehicle emissions. Thermodynamic and transport properties of binary mixtures containing Hydrocarbons and alcohols are essential in the fundamental understanding, for various engineering and industrial applications. Those properties are necessary to solve many difficult engineering problems, including heat and mass transfer, fluid flow, and energy transformations.

In this work, densities, speeds of sound and refractive indices of binary mixtures1-hexene with methanol, 1-propanol or 1-pentanol were measured in the temperature range from 293.15 to 303.15 K over the whole composition range and atmospheric pressure. From this data, excess molar volumes, deviation in speed of sound, and deviation in refractive indices, for all studied mixtures were calculated and correlated as function of temperature using Redlich-Kister polynomial equation. The density of binary mixtures of 1-hexene with alcohols was predicted using the PC-SAFT equation of state. SCFT and NR were also applied to model the experimental speed of sound data for these mixtures. Moreover, the refractive index experimental data were analyzed using widely recognized mixing rules from the literature. The excess properties of binary mixtures were found to be negative or positive curves as a function of the composition. The density of the binary mixtures has been correctly modeled with PC-SAFT. On the other hand, the 4 mixing rules used in the refractive index computation showed good quantitative agreement with the experimental data, and both SCFT and NR showed low deviations and good quantitative agreement with the experimental speed of sound.

Excess thermodynamic and transport properties of binary mixtures of furfural or furfuryl alcohol with 1-propanol and 2-propanol

A. Ayad[a,*], Z. Boudellal[a], A. Belabbaci[a],A. Negadi[a], L. Negadi[a,b]
[a] *LATA2M, Laboratoire de Thermodynamique Appliquée et Modélisation Moléculaire, University of Tlemcen, Post Office Box 119, Tlemcen 13000, Algeria*
[b] *Thermodynamics Research Unit, School of Engineering, University of KwaZulu-Natal, Howard College Campus, King George V Avenue, 4041 Durban, South Africa*
[*] *e-mail: amel.ayad@univ-tlemcen.dz*

Furfural has garnered significant interest owing to its unique physicochemical properties. It serves as a versatile platform molecule, functioning as a vital building block for fine chemical synthesis, a value-added industrial chemical, and a sustainable precursor to fuel additives.[1,2] Alcohols are widely employed as solvents and co-solvents in industrial processes. Therefore, it is particularly important to understand the properties of mixtures containing these compounds.
In this work, the excess molar volume, excess isentropic compressibility, and other excess and deviation properties of binary mixtures were investigated for the following systems: furfural (1) + 1-propanol (2), furfural (1) + 2-propanol (2), furfuryl alcohol (1) + 1-propanol (2), and furfuryl alcohol (1) + 2-propanol (2). These properties were determined from measured values of density (ρ), speed of sound (c), and refractive index (n^D) for both pure components and their mixtures at atmospheric pressure over the whole composition range at temperatures ranging from 293.15 K to 323.15 K. Excess properties were fitted to the Redlich−Kister polynomial equation. These results provide insight into the intermolecular interactions occurring in the binary mixtures.

References

(1) Gowda, A.S.; Parkin, S.; Ladipo, F.T. *Appl. Organomet. Chem.* 2012, **26**, 86−93.
(2) Yan, K.; Wu, G.; Lafleur, T.; Jarvis, C. *Renew. Sustain. Energy Rev.* 2014, **38**, 663−676.

Thermophysical properties of binary systems containing 2-ethoxyethanol and alcohols

N. L. Benkelfat-Seladji [a], N. Chiali-BabaAhmed [a], A. Ayad[a,*], A. Negadi [a], L. Negadi [a,b]

[a] *LATA2M, Laboratoire de Thermodynamique Appliquée et Modélisation Moléculaire, University of Tlemcen, Post Office Box 119, Tlemcen 13000, Algeria*

[b] *Thermodynamics Research Unit, School of Engineering, University of KwaZulu-Natal, Howard College Campus, King George V Avenue, 4041 Durban, South Africa*

[*] *e-mail: amel.ayad@univ-tlemcen.dz*

The aim of our research is to investigate the behavior of molecular interactions in liquid binary mixtures of glycol ethers such as 2-ethoxyethanol (or 2EE) and several alcohols including methanol, ethanol, 1-propanol, 2-propanol, and 2-butanol. To this end, density measurements were carried out for the pure components and their mixtures in the temperature range from 293.15 K to 323.15 K as a function of mole fraction at atmospheric pressure. The excess properties were correlated using the Redlich-Kister polynomial equation. Additionally, the density was modeled using the Cubic-Plus-Association (CPA) equation of state, which yielded excellent agreement with the experimental data.



© 2026 The JEEP226 Organizing Committee / University of Coimbra. This work is licensed under a Creative Commons Attribution-ShareAlike 4.0 International License.